
BIOGRAPHICAL SKETCH

NAME: Antonella Naldini

POSITION TITLE: Full Professor in Physiology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Start Date	Completion Date	FIELD OF STUDY
University of Siena (Italy)	Doctoral Degree	1977	1982	Pharmaceutical Chemistry
University of Siena (Italy)	Postdoctoral	1983	1985	General Physiology
University of Texas (USA)	Postdoctoral	1986	1988	Microbiology and immunology

A. Personal Statement

I am a full Professor in Physiology, within the Department of Molecular Medicine at the University of Siena and my research investigates the fundamental cellular and molecular mechanisms that regulate human health and disease. My interdisciplinary approach bridges molecular biology, biochemistry, and physiology to unravel the complexities of biological systems. During my post-doctoral training at the Department of Microbiology and Immunology at the University of Texas in Galveston, Texas, USA, I was mainly involved in studying the physiological role of cytokines. Upon returning to Siena, as a researcher in General Physiology, I directed several projects concerning the biological activities and expression of various cytokines and, more recently, cellular interactions and molecular networks associated with modifications of the extracellular microenvironment in the presence of genotoxic stress, coagulation, angiogenesis, and hypoxia. I was also a scientific consultant for a US biotech company, Chrysalis Biotechnology Inc (Galveston, Texas, USA) involved in the pharmaceutical development of a thrombin-derived peptide, TP508, which stimulates cellular events leading to angiogenesis, revascularization, and tissue repair. This could have therapeutic implications in the treatment of the recent COVID-19 pathology, having been approved in the USA for clinical trials on COVID-19 patients. My long-lasting scientific activity has led to the publication of numerous articles and invited reviews in well-recognized international journals. I am the author of over 200 scientific publications (more than 100 of them peer-reviewed with impact factor, over 100 conference abstracts, 3 book chapters) with about 4200 citations and an h-index of 37. Since 2010, I have been a "Review Editor" for Frontiers in Physiology (Vascular Physiology), and since 2017, a "Review Editor" for Frontiers in Immunology (Inflammation). I have been nominated an "ad hoc Reviewer" for the Journal of Immunology, Thrombosis and Haemostasis, Journal of Leukocyte Biology, Cancer Research, Journal of Cellular Physiology, American Journal of Respiratory and Critical Care Medicine, Journal of Thrombosis and Haemostasis, British Journal of Pharmacology, Cytokine, Clinical and Experimental Immunology, European Journal of Cancer, Carcinogenesis, Biochemical Journal, The International Journal of Biochemistry & Cell Biology, PLoS ONE, etc. More recently I am a reviewer for the MIUR (VQR) and a reviewer of various national and international research projects. I am a member of the Italian Society of Immunology, Clinical Immunology, and Allergology (SIICA), the Italian Society of Physiology, the International Cytokine Society, and the International Society of Cancer Microenvironment. I have participated in several national and international conferences and organized numerous workshops for further training of young researchers in the field of angiogenesis and immunology. From 2013 to 2019, I have been a member of the International Relations Committee of the University of Siena, representing the biomedical area and the delegate for the Erasmus project (Erasmus plus for internships) and for international relations of the Department of Molecular and Developmental Medicine.

During the years I have supervised numerous students (Bachelor's degrees, Master's degrees, and PhD students) for their theses and, throughout her academic career, I have been a committee member of several doctoral schools at the Universities of Siena and Florence. From 2014 to 2020, I coordinated the PhD School in Molecular Medicine at the University of Siena together with the Universities of Florence and Pisa, in collaboration with the Tuscany Region (Pegaso Project, International PhD Schools). I am still Faculty member of the PhD School in Molecular Medicine at the University of Siena and from 2023 also of the Doctorate in Clinical and Experimental Pharmacology at Mario Negri Institute, Milan, Italy. In the past 20 years, I have been the principal investigator and/or coordinator of research projects funded exclusively through competitive (national and international) peer-reviewed calls. More recently I have been funded by PNRR "National Center for Gene Therapy and Drugs based on RNA Technology".

B. Positions, Scientific Appointments and Honors

2019-present Full Professor in Physiology
 2004- 2019 Associate Professor (tenure) in Physiology at the Department of Molecular and Developmental Medicine, University of Siena.
 2014- 2020 Director of the PhD School in Molecular Medicine at the University of Siena, in partnership with the Universities of Florence and Pisa (International PhD Programme, Pegaso, Regione Toscana)
 2001-2004 Associate Professor of Physiology, at the Institute of General Physiology, University of Siena
 1994-2001: Assistant Professor of Physiology (tenure), at the Institute of General Physiology, University of Siena.
 1991-1993: Assistant Professor of Physiology, at the Institute of General Physiology, University of Siena.
 1990-1991: Lecturer at the University of Siena, Integrative Course of General Physiology on immunomodulators

C. Contributions to Science

1. I have published more than 100 articles in peer-reviewed journals with more than 4000 citations (h-index 37) (Google Scholar).

My early publications directly addressed the role of hypoxia in terms of cytokines production in human peripheral mononuclear cells, in addition to their role in angiogenesis.

- a) **Naldini, A.**, Carney, D. H., Bocci, V., Klimpel, K. D., Asuncion, M., Soares, L. E., & Klimpel, G. R. (1993). Thrombin enhances T cell proliferative responses and cytokine production. *Cellular immunology*, 147(2), 367-377.
- a) **Naldini, A.**, Carraro, F., Silvestri, S., & Bocci, V. (1997). Hypoxia affects cytokine production and proliferative responses by human peripheral mononuclear cells. *Journal of cellular physiology*, 173(3), 335-342.
- b) **Naldini, A.**, Sower, L., Bocci, V., Meyers, B., & Carney, D. H. (1998). Thrombin receptor expression and responsiveness of human monocytic cells to thrombin is linked to interferon-induced cellular differentiation. *Journal of cellular physiology*, 177(1), 76-84.
- c) **Naldini, A.**, Pucci, A., & Carraro, F. (2001). Hypoxia induces the expression and release of interleukin 1 receptor antagonist in mitogen-activated mononuclear cells. *Cytokine*, 13(6), 334-341.
- d) **Naldini, A.**, Pucci, A., Bernini, C., & Carraro, F. (2003). Regulation of angiogenesis by Th1-and Th2-type cytokines. *Current pharmaceutical design*, 9(7), 511-519.
- e) **Naldini, A.**, & Carraro, F. (2005). Role of inflammatory mediators in angiogenesis. *Current Drug Targets-Inflammation & Allergy*, 4(1), 3-8.

2. Later, I significantly contributed to the understanding of the physiological roles of hypoxia on various cell types including immune cells, such as monocytes and dendritic cells. My research focused on their function in immune response modulation, which was fundamental in laying the groundwork for later studies on cytokine behavior in various pathological conditions

- a) **Naldini, A.**, Filippi, I., Miglietta, D., Moschetta, M., Giavazzi, R., & Carraro, F. (2010). Interleukin-1 β regulates the migratory potential of MDAMB231 breast cancer cells through the hypoxia-inducible factor-1 α . *European Journal of Cancer*, 46(18), 3400-3408.

- b) Filippi, I., Morena, E., Aldinucci, C., Carraro, F., Sozzani, S., & **Naldini, A.** (2014). Short-term hypoxia enhances the migratory capability of dendritic cells through HIF-1 α and PI3K/Akt pathway. *Journal of cellular physiology*, 229(12), 2067-2076.
- c) Salvi, V., Vermi, W., Gianello, V., Lonardi, S., Gagliostro, V., **Naldini, A.**, ... & Bosisio, D. (2016). Dendritic cell-derived VEGF-A plays a role in inflammatory angiogenesis of human secondary lymphoid organs and is driven by the coordinated activation of multiple transcription factors. *Oncotarget*, 7(26), 39256.

3. More recently, my publications addressed the impact of hypoxia in different cell models including tumor cells as well as healthy monocytes/dendritic cell lines. In these publications we found that hypoxia can promote autophagy in human monocyte-derived dendritic cells, suggesting that dendritic cell autophagy is tightly related to tissue localization, physio-pathological conditions, and relative local oxygen tensions. We also unveiled that carbonic anhydrase expression was linked to a pathway well known for driving breast cancer and melanoma, such as Sonic Hedgehog. These studies contributed to understanding the complexity of tumors to find new therapeutic targets.

- a) Guerrini, G., Durivault, J., Filippi, I., Criscuoli, M., Monaci, S., Pouyssegur, J., **Naldini, A.**, Carraro, F., & Parks, S. K. (2019). Carbonic anhydrase XII expression is linked to the suppression of Sonic hedgehog ligand expression in triple-negative breast cancer cells. *Biochemical and biophysical research communications*
- a. Giuntini, G., Monaci, S., Cau, Y., Mori, M., **Naldini, A.**, & Carraro, F. (2020) Inhibition of melanoma cell migration and invasion targeting the hypoxic tumor-associated CAXII. *Cancers*
- b. Criscuoli, M., Ulivieri, C., Filippi, I., Monaci, S., Guerrini, G., Crifò, B., De Tommaso, D., Pelicci, G., Baldari, C., Taylor, C.T., Carraro, F., & **Naldini, A.** (2020). The Shc protein Rai enhances T-cell survival under hypoxia. *Journal of Cellular Physiology*
- c. Monaci, S., Aldinucci, C., Rossi, D., Giuntini, G., Filippi, I., Ulivieri, C., Marotta, G., Sozzani, S., Carraro, F., & **Naldini, A.** (2020) Hypoxia shapes autophagy in LPS- activated dendritic cells. *Frontiers in Immunology*

4. In addition to the contributions described above, I further explored the multitude of processes that regulate dendritic cell physiology. This body of work documented that a network of pathways and molecules are crucial for monocyte-derived dendritic cell physiology in terms of cell survival/autophagy. Of interest, I further demonstrated the role of hypoxia in regulating the described processes, highlighting the importance of this physiological process in immune cells.

- a. Monaci, S., Coppola, F., Giuntini, G., Roncoroni, R., Acquati, F., Sozzani, S., ... & **Naldini, A.** (2021). Hypoxia Enhances the Expression of RNASET2 in Human Monocyte-Derived Dendritic Cells: Role of PI3K/AKT Pathway. *International journal of molecular sciences*
- b. Monaci, S., Coppola, F., Rossi, D., Giuntini, G., Filippi, I., Marotta, G., ... & **Naldini, A.** (2022). Hypoxia Induces Autophagy in Human Dendritic Cells: Involvement of Class III PI3K/Vps34. *Cells*
- c. Coppola, F., Monaci, S., Falsini, A., Aldinucci, C., Filippi, I., Rossi, D., ... & **Naldini, A.** (2024). SQSTM1/p62 inhibition impairs pro-survival signaling in hypoxic human dendritic cells. *Biochimica et Biophysica Acta (BBA)-Molecular Cell Research*, 1871(2), 119625.