
BIOGRAPHICAL SKETCH

NAME **Antonio Musarò, Ph.D.**

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POSITION TITLE: Full Professor

Professor of Histology and Embryology

Professor of Biotechnology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Sapienza University of Rome, Biological Science.	Biology	1991	Muscle Biology
Sapienza University of Rome, Medical School	Ph.D.	1996	Biotechnological Sciences
Harvard University, Boston, USA	Research Fellow in Medicine	1996-2000	Molecular biology of aging

A. Personal Statement

The overall goal of my research program is to characterize the cellular, molecular and functional aspects of muscle homeostasis and regeneration. Specifically, my research focuses in three areas: (1) Modulation of hostile microenvironment to improve stem cell-mediated therapy; (2) characterization of the physiopathologic interplay between muscle and nerve; (3) establishment of muscle engineered *in vitro* model to study muscle homeostasis and differentiation. In particular, in my lab, we study the molecular mechanisms involved in the growth, maturation and hypertrophy of skeletal muscle. Our expertise lies in the design, generation and analysis of *in vivo* experimental models for the development of therapeutic approaches for the prevention/treatment of neuromuscular disorders, including Duchenne Muscular Dystrophy.

B. Positions and Honors

Positions and Employment

1996–2000	Postdoctoral training– Research fellow, Cardiovascular Research Center; Harvard University.
1999–2007	Assistant professor, Sapienza University of Rome –Medical School.
2002	Visiting Professor, Edith Cowan University, Australia.
2003– present	Professor of Biotechnology; Sapienza University of Rome.
2003–2014	Adjunct Associate Professor (honorary position), School of Biomedical & Sports Science; Faculty of Computing, Health and Science. Edith Cowan University; Western Australia.
2015-2020	Professor of Histology, nursing school- Cassino-Sapienza University.
2016-2020	Junior Research Fellow, Scuola Superiore di Studi Avanzati Sapienza.
2007- Jan 2017	Associate professor, Medical and Biotechnology School, Sapienza University of Rome.
Feb 2017-present	Full professor, Medical and Biotechnology School, Sapienza University of Rome
2018-2024	Coordinator of the Ph.D. program in Morphogenesis and Tissue Engineering
2018-2022	Director of Master in Stem cells and genome editing

2020-present	Senior Research Fellow and Coordinator of Life Science academic class, Sapienza School for Advanced Studies (SSAS)
2024-	Director of Master in One Health, Sapienza University of Rome

Other Experience and Professional Memberships

2001-present	Expert reviewer for international scientific journals
2004-present	Member of the Society of Cell Biology
2005	Lecturer and Instructor of EMBO Practical Course: From Mice to Cells
2010-2017	Member of the editorial board of World Journal of Biological Chemistry
2010-present	Scientific director of "Festa della Scienza"
2010-present	Member of the editorial board of Skeletal Muscle
2011-2023	Member of the editorial board of PlosOne
2011-2016	Chief of Interuniversity Institute of Myology (IIM)
2015-2023	Member of the editorial board of Current Genomics
2019-2023	Academic editor of Cells
2014-present	Academic Member of Accademia Medica di Roma
2018-present	Board member of Accademia Medica di Roma

Honours

2001	Honour for advance in Biological Research
2003	Award for Scientific Communication (Rotary Club)
2006	Award for Scientific Communication, Foglia di Tabacco
2009	Award Sapienza Ricerca for best research 2009 (Sapienza University of Rome)
2014	La Plejade ANCIS International Award 2014 for Scientific Research
2018	Unitel-Puglia (Pergamena D'onore)
2021	Award "Union Invictus" for scientific career (PassioneSport.tv)
2024	Award «Alfredo Margreth» for Cell Biology, Accademia Nazionale dei Lincei

C. Contributions to Science

Aging and neuromuscular diseases (ALS, muscular dystrophies); role of stem cells and tissue niche on muscle regeneration.

1. Characterization of the roles of IGF-1 in skeletal muscle homeostasis, regeneration, and diseases. Focusing on specific pathways controlling muscle growth and regeneration, I carefully constructed a program of basic research to characterize the role of specific isoforms of insulin-like growth factor (IGF-1) in the physiopathology of skeletal muscle and in muscle pathologies. We made significant contributions in the field of muscle hypertrophy and muscle aging and contributed to identify signalling pathways involved in skeletal muscle regeneration and diseases. We demonstrated an essential role of inflammatory response in muscle regeneration and repair and characterized the specific role of IGF-1 in the modulation of the tissue niche and on the recruitment of stem cells into the injured muscle.

- a) Musarò A, McCullagh KJ, Naya FJ, Olson EN, Rosenthal N. IGF-1 induces skeletal myocyte hypertrophy through calcineurin in association with GATA-2 and NF-ATc1. *Nature*. 1999; 400: 581-5.
- b) Musarò A, McCullagh K, Paul A, Houghton L, Dobrowolny G, Molinaro M, Barton ER, Sweeney HL, Rosenthal N. Localized Igf-1 transgene expression sustains hypertrophy and regeneration in senescent skeletal muscle. *Nature Genetics* 2001; 27: 195-200.
- c) Pelosi L, Giacinti C, Nardis C, Borsellino G, Rizzuto E, Nicoletti C, Wannenes F, Battistini L, Rosenthal N, Molinaro M, Musarò A. Local expression of IGF-1 accelerates muscle regeneration by rapidly modulating inflammatory cytokines and chemokines. *FASEB J*. 2007; 21(7):1393-402.

- d) Pelosi L, Coggi A, Forcina L, Musarò A. MicroRNAs modulated by local mIGF-1 expression in mdx dystrophic mice. *Front Aging Neurosci.* 2015; 7:69.
- e) Ascenzi F, Barberi L, Dobrowolny G, Villa Nova Bacurau A, Nicoletti C, Rizzuto E, Rosenthal N, Scicchitano BM, Musarò A. Effects of IGF-1 isoforms on muscle growth and sarcopenia. *Aging Cell.* 2019 Apr 5:e12954.

2. Characterization of the physiopathologic interplay between muscle and nerve. A crucial system severely affected in several neuromuscular diseases, including ALS, is the loss of effective connection between muscle and nerve, leading to a pathological non-communication between the two tissues. In the last 10 years we have made a breakthrough in research into ALS, demonstrating a key role of skeletal muscle in the pathogenesis of ALS. Our research supported the redefinition of ALS as a “multi-systemic” disease in which alterations in structural, physiological, and metabolic parameters in different cell types (muscle, motoneuron, glia) may act synergistically to exacerbate the disease.

- a) Dobrowolny G, Giacinti C, Pelosi L, Nicoletti C, Winn N, Barberi L, Molinaro M, Rosenthal N, Musarò A. Muscle expression of a local Igf-1 isoform protects motor neurons in an ALS mouse model. *J Cell Biol.* 2005;168:193-9.
- b) Dobrowolny G, Aucello M, Rizzuto E, Beccafico S, Mammucari C, Boncompagni S, Belia S, Wannenes F, Nicoletti C, Del Prete Z, Rosenthal N, Molinaro M, Protasi F, Fanò G, Sandri M, and Musarò A. Skeletal muscle is a primary target of SOD1G93A -mediated toxicity *Cell Metabolism* 2008; 8:425-36.
- c) Dobrowolny G, Martini M, Scicchitano BM, Romanello V, Boncompagni S, Nicoletti C, Pietrangelo L, De Panfilis S, Catizone A, Bouchè M, Sandri M, Rudolf R, Protasi F, Musarò A. Muscle Expression of SOD1G93A Triggers the Dismantlement of Neuromuscular Junction via PKC-Theta. *Antioxid Redox Signal.* 2018; 28:1105-1119.
- d) Dobrowolny G, Lepore E, Martini M, Barberi L, Nunn A, Scicchitano BM, Musarò A. Metabolic Changes Associated with Muscle Expression of SOD1G93A. *Front Physiol.* 2018;9:831.
- e) Musarò A, Dobrowolny G, Cambieri C, Onesti E, Ceccanti M, Frasca V, Pisano A, Cerbelli B, Lepore E, Ruffolo G, Cifelli P, Roseti C, Giordano C, Gori MC, Palma E, Inghilleri M. Neuromuscular magnetic stimulation counteracts muscle decline in ALS patients: results of a randomized, double-blind, controlled study. *Sci Rep.* 2019; 9(1):2837.
- f) Dobrowolny G, Martone J, Lepore E, Casola I, Petrucci A, Inghilleri M, Morlando M, Colantoni A, Scicchitano BM, Calvo A, Bisogni G, Chiò A, Sabatelli M, Bozzoni I, Musarò A. A longitudinal study defined circulating microRNAs as reliable biomarkers for disease prognosis and progression in ALS human patients. *Cell Death Discov.* 2021; 7(1):4. doi: 10.1038/s41420-020-00397-6.
- g) Casola I, Scicchitano BM, Lepore E, Mandillo S, Golini E, Nicoletti C, Barberi L, Dobrowolny G, Musarò A. Circulating myomiRs in Muscle Denervation: From Surgical to ALS Pathological Condition. *Cells.* 2021 Aug 10;10(8):2043. doi: 10.3390/cells10082043.

3. Define the signature of hostile microenvironment in muscular dystrophy and sarcopenia.

We study muscle homeostasis and regeneration under normal and pathologic conditions. The main goal of our project is to define the tissue signals and to characterize the molecular mechanisms of muscle wasting. Although considerable information has accumulated regarding the physiopathology of muscle diseases, the associated molecular mechanisms are still poorly understood. We recently provided evidence about specific molecules that modulate the hostile microenvironment and propose alternative pharmacological strategy for treatment muscle diseases.

- a) Cacchiarelli D, Martone J, Girardi E, Cesana M, Incitti T, Morlando M, Nicoletti C, Santini T, Sthandier O, Barberi L, Auricchio A, Musarò A, Bozzoni I. MicroRNAs involved in molecular circuitries relevant for the Duchenne muscular dystrophy pathogenesis are controlled by the dystrophin/nNOS pathway. *Cell Metab.* 2010; 12:341-51.

- b) Pelosi, L., Berardinelli MG, De Pasquale L, Nicoletti C, D'Amico A, Carvello F, Moneta GM, Catizone A, Bertini E, De Benedetti F, Musarò A. Functional and Morphological Improvement of Dystrophic Muscle by Interleukin 6 Receptor Blockade, *EBioMedicine* 2015; 2:285-93
- c) Petrillo S, Pelosi L, Piemonte F, Travaglini L, Forcina L, Catteruccia M, Petrini S, Verardo M, D'Amico A, Musarò A, Bertini E. Oxidative stress in Duchenne muscular dystrophy: focus on the NRF2 redox pathway. *Hum Mol Genet.* 2017; 26:2781-2790.
- d) Ballarino M, Cipriano A, Tita R, Santini T, Desideri F, Morlando M, Colantoni A, Carrieri C, Nicoletti C, Musarò A, Carroll DO, Bozzoni I. Deficiency in the nuclear long noncoding RNA Charmes causes myogenic defects and heart remodeling in mice. *EMBO J.* 2018 ;37. pii: e99697.
- e) Forcina L, Miano C, Scicchitano BM, Rizzuto E, Berardinelli MG, De Benedetti F, Pelosi L, Musarò A. Increased Circulating Levels of Interleukin-6 Affect the Redox Balance in Skeletal Muscle. *Oxid Med Cell Longev.* 2019; 2019:3018584.
- f) Pelosi L, Berardinelli MG, Forcina L, Ascenzi F, Rizzuto E, Sandri M, De Benedetti F, Scicchitano BM, Musarò A. Sustained Systemic Levels of IL-6 Impinge Early Muscle Growth and Induce Muscle Atrophy and Wasting in Adulthood. *Cells.* 2021 Jul 18;10(7):1816. doi: 10.3390/cells10071816.

4. Muscle engineered in vitro model to study muscle homeostasis and differentiation

In our laboratory it has been recently developed a 3-dimensional skeletal muscle construct, called eX-vivo Muscle engineered Tissue, X-MET. X-MET was obtained from murine skeletal muscle primary culture. The isolation from skeletal muscle of heterogeneous cell populations such as satellite cells, fibroblasts and endothelial cells, is a prerequisite of X-MET formation. Since the X-MET mimics the complex morphological properties of skeletal muscle tissue, it may be considered an ideal in vitro model of skeletal muscle, simplifying the study of complex processes such as muscle homeostasis, differentiation and muscle-nerve interplay under physiologic and pathologic conditions such as muscular dystrophy and ALS.

- a) Carosio S, Barberi L, Rizzuto E, Nicoletti C, Prete ZD, Musarò A. Generation of eX vivo-vascularized Muscle Engineered Tissue (X-MET). *Sci Rep.* 2013; 3:1420.
- b) Cosentino M, Nicoletti C, Valenti V, Schirone L, Di Nonno F, Apa L, Zouhair M, Genovese D, Madaro L, Dinarelli S, Rossi M, Del Prete Z, Sciarretta S, Frati G, Rizzuto E, Musarò A. Remodeled eX vivo muscle engineered tissue improves heart function after chronic myocardial ischemia. *Sci Rep.* 2023 Jun 26;13(1):10370. doi: 10.1038/s41598-023-37553-8.
- c) Cosentino M, Forcina L, Zouhair M, Apa L, Genovese D, Boccia C, Rizzuto E, Musarò A. Modelling three-dimensional cancer-associated cachexia and therapy: The molecular basis and therapeutic potential of interleukin-6 transsignaling blockade. *J Cachexia Sarcopenia Muscle.* 2023;14(6):2550-2568. doi: 10.1002/jcsm.13329.

Patents

- 1. Rosenthal N, Harvey RP, Palmer S, Musarò A, inventors; Novel molecules expressed during muscle development and genetic sequences encoding the same. (PCT/AU1999/000220).
- 2. Rosenthal N, Musarò A, Nadine Winn, inventors; IGF-1 novel peptides. (PCT/IB2005/003953.)
- 3. Osta Pinzolas R, Rando Zalduendo A, Toivonen J, Zaragoza P, Musarò A. Compositions for the treatment of motor neuron diseases. (PCT/ES2015/070896).