

C.V. MUSARO' ANTONIO

BIOGRAPHICAL SKETCH

MUSARO' Antonio Lab web site: http://musarolab-uniroma1.jimdo.com/ Antonio Musarò web site: https://sites.google.com/a/uniroma1.it/antoniomusaro/ Orcid: 0000-0002-2944-9739 Scopus ID: 6602410173	POSITION TITLE Full Professor Professor of Histology and Embryology Professor of Biotechnology
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EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	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. Positions and Honours

Positions and Employment

1996–2000	Postdoctoral training– Research fellow, Cardiovascular Research Center; Harvard University.
1999–2007	Assistant professor, Sapienza University of Rome –Medical School.
1999-present	Professor of Histology and Embryology, Medical School, Sapienza University of Rome. Member of the academic committee of PhD program in Morphogenesis & Tissue Engineering
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-present	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)

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-present	Member of the editorial board of PlosOne
2015-present	Member of the editorial board of Current Genomics
2019-present	Academic editor of Cells
2014-present	Academic Member of Accademia Medica di Roma
2018-present	Board member of Accademia Medica di Roma
2011-2016	Chief of Interuniversity Institute of Myology (IIM)

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)

B. Major Research Interests and 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.

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, motorneuron, glia) may act synergistically to exacerbate the disease.

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.

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.

C. Publications (h index = 43 by Scopus and WoS; 51 by Google Scholar)

1. Germani A., Fusco C., Martinotti S., Musarò A., Molinaro M., Zani BM. TPA-induced differentiation of human rhabdomyosarcoma cells involves dephosphorylation and nuclear accumulation of mutant p53. *Biochem Biophys Res Commun.* 1994, 202:17-24.
2. Musarò A., Cusella De Angelis MG, Germani A., Ciccarelli C., Molinaro M., Zani BM; Enhanced expression of myogenic regulatory genes in aging skeletal muscle *Exp Cell Res.* 1995; 221:241-8.
3. Barton-Davis ER, Shoturma DI, Musarò A, Rosenthal N, Sweeney HL. Viral mediated expression of insulin-like growth factor I blocks the aging-related loss of skeletal muscle function. *Proc Natl Acad Sci U S A.* 1998 95(26):15603-7.
4. Musarò A., Rosenthal N. Maturation of the myogenic program is induced by postmitotic expression of insulin-like growth factor I. *Mol Cell Biol.* 1999 19:3115-24.
5. Musarò A., Rosenthal N. Transgenic mouse models of muscle aging. *Exp Gerontol.* 1999; 34(2):147-56. Review.
6. 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.
7. Tsao L, Neville G, Musarò A, McCullagh KJ, Rosenthal N. Revisiting calcineurin and human heart failure. *Nature Medicine* 2000; 6: 2-3.
8. 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.
9. Barton ER, Morris L., Musarò A., Rosenthal N., and Sweeney H.L. Muscle specific expression of Insulin-like Growth Factor I counters muscle decline in mdx mice. *J.Cell Biol.* 2002; 157: 137-147.
10. Scicchitano BM, Spath L, Musarò A, Molinaro M, Adamo S, and Nervi C. The Myocyte Enhancer Factor 2 is Essential for Myogenin Expression during AVP Induced Myogenesis. *J. Endocrinology* 2002; 16: 1407-16.

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11. Musarò A. and Rosenthal N. The role of local Insulin-like Growth Factor-1 isoforms in the pathophysiology of skeletal muscle. *Current Genomics* 2002; 3: 149-162.
12. Rosenthal, N, Musarò A. Gene therapy for cardiac cachexia? *International Journal of Cardiology* 2002 85: 185-191
13. Winn N., Paul A., Musarò A., Rosenthal N. Insulin-like Growth Factor isoforms in skeletal muscle aging, regeneration and disease. *Cold Spring Harbor Symposia on Quantitative Biology*. 2002; LXVII: 507-518.
14. Musarò A, Rosenthal N. Attenuating muscle wasting: cell and gene therapy approaches. *Current Genomics* 2003; 4:575-585.
15. Bertini E, Biancalana V, Bolino A, Buj Bello A, Clague M, Guicheney P, Jungbluth H, Kress W, Musarò A, Nandurkar H, Pirola L, Romero N, Senderek J, Suter U, Sewry C, Tronchere H, Wallgren-Pettersson C, Wishart MJ, Laporte J. 118th ENMC International Workshop on Advances in Myotubular Myopathy. 26-28 September 2003, Naarden, The Netherlands. (5th Workshop of the International Consortium on Myotubular Myopathy). *Neuromuscul Disord*. 2004 14:387-96.
16. Musarò A, Giacinti C, Borsellino G, Dobrowolny G, Pelosi L, Cairns L, Ottolenghi S, Bernardi G, Cossu G, Battistini L, Molinaro M, Rosenthal N. Muscle restricted expression of mIGF-1 enhances the recruitment of stem cells during muscle regeneration. *Proc Natl Acad Sci U S A* 2004; 101: 1206-1210.
17. 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.
18. Scicchitano BM, Spath L, Musarò A, Molinaro M, Rosenthal N, Nervi C, Adamo S. Vasopressin-dependent Myogenic Cell Differentiation Is Mediated by Both Ca²⁺/Calmodulin-dependent Kinase and Calcineurin Pathways. *Mol Biol Cell*. 2005; 16:3632-41.
19. Musarò A. Growth factor enhancement of muscle regeneration: a central role of IGF-1. *Arch Ital Biol*. 2005; 143:243-8
20. Denti MA, Rosa A, D'Antona G, Sthandier O, De Angelis FG, Nicoletti C, Allocca M, Pansarasa O, Parente V, Musarò A, Auricchio A, Bottinelli R, Bozzoni I. Body-wide gene therapy of Duchenne muscular dystrophy in the mdx mouse model. *Proc Natl Acad Sci U S A*. 2006; 103:3758-63.
21. Denti MA, Rosa A, D'Antona G, Sthandier O, Angelis FG, Nicoletti C, Allocca M, Pansarasa O, Parente V, Musarò A, Auricchio A, Bottinelli R, Bozzoni I. Chimeric Adeno-Associated Virus/Antisense U1 Small Nuclear RNA Effectively Rescues Dystrophin Synthesis and Muscle Function by Local Treatment of mdx Mice. *Human Gene Ther*. 2006 17: 1-10.
22. Musarò A., Dobrowolny G., Rosenthal N. The neuroprotective effects of a locally acting IGF-1 isoform. *Experimental Gerontology* 2007; 42:76-80.
23. Rosenthal N, Santini MP, Musarò A. Growth factor enhancement of cardiac regeneration. *Cell Transplant*. 2006;15 Suppl 1:S41-5.
24. Musarò A., Rosenthal N. The critical role of Insulin-like Growth Factor-1 isoforms in the physiopathology of skeletal muscle. *Current Genomics* 2006; 3: 19-32.
25. 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; 21:1393-402.
26. Musarò A., Giacinti C., Pelosi L., Dobrowolny G., Barberi L., Nardis C., Coletti D., Scicchitano B.M., Adamo S., Molinaro M.. Stem Cell-mediated muscle regeneration and repair in aging and neuromuscular diseases. *European Journal of Histochemistry*. 2007; 51 Suppl 1:35-43.
27. Fanzani A, Musarò A, Stoppani E, Giuliani R, Colombo F, Preti A, Marchesini S. Hypertrophy and atrophy inversely regulate Caveolin-3 expression in myoblasts. *Biochem Biophys Res Commun*. 2007; 357:314-8.
28. Pelosi M, Marampon F, Zani BM, Prudente S, Perlas E, Caputo V, Cianetti L, Berno V, Narumiya S, Kang SW, Musarò A, Rosenthal N. ROCK2 and its alternatively spliced isoform ROCK2m positively control the maturation of the myogenic program. *Mol Cell Biol*. 2007; 27:6163-76.
29. Dobrowolny G, Aucello M, Molinaro M, Musarò A. Local expression of mIgf-1 modulates ubiquitin, caspase and CDK5 expression in skeletal muscle of an ALS mouse model. *Neurol Res*. 2008; 30:131-6.
30. Del Prete Z, Musarò A, Rizzuto E. Measuring Mechanical Properties, Including Isotonic Fatigue, of Fast and Slow MLC/mIgf-1 Transgenic Skeletal Muscle. *Ann Biomed Eng*. 2008; 36:1281-90.
31. Denti M A, Incitti T, Sthandier O, Nicoletti C, De Angelis F, Rizzuto E, Auricchio A, Musarò A, Bozzoni I. Long-term benefit of AAV/antisense-mediated exon skipping in dystrophic mice. *Human Gene Therap*. 2008; 19:601-8.
32. Giacinti C, Musarò A, De Falco G, Jourdan I, Molinaro M, Bagella L, Simone C, Giordano A. Cdk9-55: A new player in muscle regeneration. *J Cell Physiol*. 2008; 216:576-82.
33. 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.
34. Aucello M, Dobrowolny G, Musarò A. Localized accumulation of oxidative stress causes muscle atrophy through activation of an autophagic pathway. *Autophagy*. 2009; 5:527-9.

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35. Palazzolo I., Stack C., Kong L., Musaro A., Adachi H., Katsuno M., Sobue G., Taylor J.P., Sumner C., Fischbeck K., and Pennuto M. Overexpression of IGF-1 in Muscle Attenuates Disease in a Mouse Model of Spinal and Bulbar Muscular Atrophy. *Neuron* 2009; 63:316-28.
36. Rizzuto E, Musarò A, Catizone A, Del Prete Z. Measuring tendon properties in mdx mice: Cell viability and viscoelastic characteristics. *J. Biomech.* 2009; 42:2243-8.
37. Colombini B, Benelli G, Nocella M, Musarò A, Cecchi G, Bagni MA. Mechanical properties of intact single fibres from wild-type and MLC/mlgf-1 transgenic mouse muscle. *J Muscle Res Cell Motil.* 2009; 30:199-207.
38. Scicchitano BM, Rizzuto E, and Musarò A. Counteracting muscle wasting in aging and neuromuscular diseases: the critical role of IGF-1. *Aging* 2009; 1: 451-457.
39. Messina S, Bitto A, Aguenouz M, Mazzeo A, Migliorato A, Polito F, Irrera N, Altavilla D, Vita GL, Russo M, Naro A, De Pasquale MG, Rizzuto E, Musarò A, Squadrito F, Vita G. Flavocoxid counteracts muscle necrosis and improves functional properties in mdx mice: a comparison study with methylprednisolone. *Exp Neurol.* 2009; 220:349-58.
40. Musarò A, Fulle S and Fanò G. Oxidative stress and muscle homeostasis. *Curr Opin Clin Nutr Metab Care* 2010; 13:236-42.
41. Melchionna R, Di Carlo A, De Mori R, Cappuzzello C, Barberi L, Musarò A, Cencioni C, Fujii N, Tamamura H, Crescenzi M, Capogrossi MC, Napolitano M, Germani A. Induction of myogenic differentiation by SDF-1 via CXCR4 and CXCR7 receptors. *Muscle Nerve.* 2010; 41:828-35.
42. Musaro A. Comments on Point:Counterpoint: IGF is/is not the major physiological regulator of muscle mass. The strange case of IGF-1. *J Appl Physiol.* 2010; 108:1826.
43. 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.
44. Vinciguerra M, Musaro A, Rosenthal N. Regulation of muscle atrophy in aging and disease. *Adv Exp Med Biol.* 2010; 694:211-33.
45. Musarò A. State of the art and the dark side of amyotrophic lateral sclerosis *World J Biol Chem.* 2010; 1: 62-68.
46. Bosch-Marcé M, Wee CD, Martinez TL, Lipkes CE, Choe DW, Kong L, Vanmeerbeke JP, Musarò A, Sumner CJ. Increased IGF-1 in muscle modulates the phenotype of severe SMA mice. *Hum Mol Genet.* 2011 20:1844-53.
47. Carosio S, Berardinelli MG, Aucello M, Musarò A. Impact of ageing on muscle cell regeneration. *Ageing Res Rev.* 2011;10:35-42.
48. Dobrowolny G, Aucello M, Musarò A. Muscle atrophy induced by SOD1G93A expression does not involve the activation of caspase in the absence of denervation. *Skelet Muscle.* 2011;1(1):3.
49. Toschi A, Severi A, Coletti D, Catizone A, Musarò A, Molinaro M, Nervi C, Adamo S, Scicchitano BM. Skeletal muscle regeneration in mice is stimulated by local overexpression of v1a-vasopressin receptor. *Mol Endocrinol.* 2011; 25:1661-73.
50. Kuraitis D, Zhang P, Zhang Y, Padavan DT, McEwan K, Sofrenovic T, McKee D, Zhang J, Griffith M, Cao X, Musarò A, Ruel M, Suuronen EJ. A stromal cell-derived factor-1 releasing matrix enhances the progenitor cell response and blood vessel growth in ischaemic skeletal muscle. *Eur Cell Mater.* 2011; 22:109-23.
51. Forte G, Pietronave S, Nardone G, Zamperone A, Magnani E, Pagliari S, Pagliari F, Giacinti C, Nicoletti C, Musaró A, Rinaldi M, Ribezzo M, Comoglio C, Traversa E, Okano T, Minieri M, Prat M, Di Nardo P. Human cardiac progenitor cell grafts as unrestricted source of supernumerary cardiac cells in healthy murine hearts. *Stem Cells.* 2011;29:2051-61.
52. Kern H, Pelosi L, Coletto L, Musarò A, Sandri M, Vogelauer M, Trimmel L, Cvecka J, Hamar D, Kovarik J, Löfler S, Sarabon N, Protasi F, Adami N, Biral D, Zampieri S, Carraro U. Atrophy/hypertrophy cell signaling in muscles of young athletes trained with vibrational-proprioceptive stimulation. *Neurol Res.* 2011; 33:998-1009.
53. Kuraitis D, Giordano C, Ruel M, Musarò A, Suuronen EJ. Exploiting extracellular matrix-stem cell interactions: A review of natural materials for therapeutic muscle regeneration. *Biomaterials.* 2012; 33:428-43.
54. Sandonà D, Desaphy JF, Camerino GM, Bianchini E, Ciciliot S, Danieli-Betto D, Dobrowolny G, Furlan S, Germinario E, Goto K, Gutschmann M, Kawano F, Nakai N, Ohira T, Ohno Y, Picard A, Salanova M, Schiffl G, Blottner D, Musarò A, Ohira Y, Betto R, Conte D, Schiaffino S. Adaptation of Mouse Skeletal Muscle to Long-Term Microgravity in the MDS Mission. *PLoS One.* 2012; 7:e33232.
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56. Murdocca M, Malgieri A, Luchetti A, Saieva L, Dobrowolny G, De Leonibus E, Filareto A, Quitadamo MC, Novelli G, Musarò A, Sangiuolo F. IPLEX administration improves motor neuron survival and ameliorates motor functions in a severe mouse model of SMA. *Mol Med.* 2012 Sep 25; 18:1076-85.
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61. Musarò A. Understanding ALS: new therapeutic approaches. *FEBS J.* 2013; 280:4315-22.
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C.1 Book chapters

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D. 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).