

Stefano Schiaffino

Professor Emeritus, University of Padova

Emeritus, Veneto Institute of Molecular Medicine (VIMM)

Education

M.D. University of Modena, 1963

Positions

2000-17 Group leader and Vice-President, Veneto Institute of Molecular Medicine (VIMM), Padova
1987-2010 Director, CNR Center of Muscle Biology and Physiopathology, Padova
1986-87 Visiting professor, INSERM U127 (Hôpital Lariboisière) and Institut Pasteur, Paris
1981-2010 Full Professor of General Pathology, School of Medicine, University of Padova
1971-81 Associate Professor of General Pathology, School of Medicine, Univ. Padova
1965-71 Assistant Professor of General Pathology, School of Medicine, Univ. Padova

Honors

1997 *Doctor honoris causa* in Medicine, Université Paris 7 - Denis Diderot, Paris
1988 *Doctor honoris causa* in Medicine, University of Umeå (Sweden)

Academies

Accademia dei Lincei (Roma), Istituto Veneto di Scienze, Lettere ed Arti (Venezia), *Accademia Europaea*

Selected publications (before 2011)

Full list: <https://scholar.google.com/citations?user=x8Y43UYAAAAJ&hl=en>

Masiero E ... Schiaffino S, Sandri M (2009) Autophagy is required to maintain muscle mass. *Cell Metab* 10:507-15.
Blaauw B ... Schiaffino S (2008) Akt activation prevents the force drop induced by eccentric contractions in dystrophin-deficient skeletal muscle. *Hum Mol Genet* 17:3686-96.
Mammucari C ... Schiaffino S, Sandri M (2007) FoxO3 controls autophagy in skeletal muscle in vivo. *Cell Metab* 6:458-471.
McCullagh K ... Schiaffino S (2004) NFAT is a nerve activity sensor and controls activity-dependent myosin switching. *Proc Nat Acad Sci USA* 101:10590-95.
Sandri M ... Schiaffino S, Lecker SH, Goldberg AL (2004) Foxo transcription factors induce the atrophy-related ubiquitin ligase atrogin-1 and cause skeletal muscle atrophy. *Cell* 117:399-412.
Pallafacchina G ... Schiaffino S (2002) A protein kinase B-dependent and rapamycin-sensitive pathway controls skeletal muscle growth but not fiber type specification. *Proc Nat Acad Sci USA* 99:9213-18.
Serrano AL ... Schiaffino S (2001) Nerve activity- dependent specification of slow skeletal muscle fibers is controlled by calcineurin. *Proc Nat Acad Sci USA* 98:13108-13.
Murgia M ... Schiaffino S (2000) Ras is involved in nerve-activity- dependent regulation of muscle genes. *Nature Cell Biol* 2:142-147.
Schiaffino S, Reggiani C. (1996) Molecular diversity of myofibrillar proteins: gene regulation and functional significance. *Physiol Rev* 76:371-423.
De Nardi C ... Schiaffino S (1993) Type 2X myosin heavy chain is coded by a muscle fiber type-specific and developmentally regulated gene. *J Cell Biol*. 123:823-835.
Lyons G, Schiaffino S, ... Buckingham M (1990) Developmental regulation of myosin gene expression in mouse cardiac muscle. *J Cell Biol* 111: 2427-2436.
Schiaffino S ... Lømo T (1989) Three myosin heavy chain isoforms in type 2 skeletal muscle fibres. *J Muscle Res Cell Motil* 10:197-205.
Schiaffino S, Samuel JL ... Schwartz K (1989) Non-synchronous accumulation of alpha-skeletal actin and beta-myosin heavy chain mRNAs during early stages of pressure overload-induced cardiac hypertrophy demonstrated by in situ hybridization. *Circ Res* 64:937- 948.
Sartore S, Gorza L, Schiaffino S (1982). Fetal myosin heavy chains in regenerating muscle. *Nature* 298:294-296.
Gorza L, Sartore S, Schiaffino S (1982). Myosin types and fiber types in cardiac muscle. 2. Atrial myocardium. *J Cell Biol* 95 838-845.
Sartore S ... Schiaffino S (1981). Myosin types and fiber types in cardiac muscle. 1. Ventricular myocardium. *J Cell Biol* 88:226-233.
Sartore S, Pierobon Bormioli S, Schiaffino S (1978). Immunohistochemical evidence for myosin polymorphism in the chicken heart. *Nature* 274:82-83.
Schiaffino S, Hanzlikova V (1972). Autophagic degradation of glycogen in skeletal muscles of the newborn rat. *J Cell Biol* 52:41-51.
Schiaffino S, Hanzlikova V. Pierobon Bormioli S (1970). Relations between structure and function in rat skeletal muscle fibers. *J Cell Biol* 47:107-115.

Schiaffino S, Margreth A (1969). Coordinated development of the sarcoplasmic reticulum and T system during postnatal development of rat skeletal muscle. *J Cell Biol* 41:855-875.

Books

Schiaffino S & Partridge T, eds. (2008) Skeletal muscle repair and regeneration. Springer Netherlands, pp. XIV-380.
Schiaffino S (1992) Problemi di Patologia e Fisiopatologia. Edizioni Libreria Progetto, Padova, pp. 7-261.

MAJOR ACHIEVEMENTS

I initially studied the diversity of skeletal muscle fibers using EM and immunohistochemical approaches using specific anti-myosin polyclonal and monoclonal antibodies prepared in our lab. A major result of these studies has been the identification of regenerating muscle fibers based on the expression of a developmental form of myosin (*Nature* 1982). Another important result has been the discovery of a novel fast-type myosin, called type 2X, coded by a distinct gene, and a corresponding fiber type in mammalian skeletal muscle (*JMRCM* 1989; *J Cell Biol* 1993). During these studies, we serendipitously found that cardiac muscle cells are also heterogeneous in term of myosin composition, thus providing specific molecular markers that for the first time allowed to distinguish between muscle cell populations in atrial and ventricular myocardium and heart conduction tissue (*Nature* 1978). After a sabbatical in Paris, where I worked in Ketty Schwartz and Margaret Buckingham labs, I started molecular biology analyses of myosin and troponin muscle genes in skeletal and cardiac muscle. I subsequently shifted my research activity to cell signaling in adult skeletal muscle, focusing on the mechanisms that control fiber type specification and muscle hypertrophy and atrophy. Using an *in vivo* transfection approach, aimed at generating selective perturbations of different signaling pathways with constitutively active constructs or RNAi approaches, we were able to identify specific pathways that modulate muscle fiber size and fiber type (*Nat Cell Biol* 2000; *Proc Natl Acad Sci USA* 2001 & 2002). In collaboration with Alfred Goldberg and Marco Sandri we have defined the role of the transcription factor FoxO in protein degradation via the ubiquitin proteasomal and autophagic/lysosomal pathways (*Cell* 2004, *Cell Metab* 2007 & 2009).

ACTIVITIES FOR THE SCIENTIFIC COMMUNITY

Venetian Institute of Molecular Medicine (VIMM)

In 2000 I founded with some colleagues of the University of Padova a private research center, the Venetian Institute of Molecular Medicine (VIMM) and have been acting as Vice-President of this institute for many years. The mission of the center is to study the signaling pathways that underpin normal and pathological cell function and to promote the interaction between basic and clinical scientists.

Generation of anti-myosin monoclonal antibodies

Hybridomas secreting anti-myosin monoclonal antibodies were generated in my lab and donated to the Developmental Studies Hybridoma Bank (DSHB), a National Resource created by NIH. Some of these antibodies (BA-D5, SC-71 and BF-F3) are widely used for fiber typing in skeletal muscle and are among the most requested in the DSHB collection.

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Activity report as Professor Emeritus (2011-present)

Visiting Professor

- October-November 2024: CECAD, University of Cologne (lab Marcus Krueger)
- September-November 2022: Waseda University, Tokyo (lab Takayuki Akimoto)
- March-June 2019: Inserm UMR 942, Hôpital Lariboisière, Paris (lab Jane Lise Samuel)
- December 2018: Pompeu Fabra University, Barcelona (lab Pura Munoz-Canoves)
- August-November 2018: University of Copenhagen (lab Abigail Mackey & Michael Kjaer)

Major projects and research papers (corresponding author in bold)

During this period, I was involved in four major projects: i) circadian rhythms in skeletal muscle, ii) the role of the MRF4-MEF2 axis in the control of muscle growth, iii) single muscle fiber proteomics and iv) omics analyses of the human myotendinous junction. In addition, I wrote several reviews, mostly on muscle fiber types and muscle atrophy/hypertrophy, including a highly cited review in *Physiological Reviews*.

Circadian rhythms in skeletal muscle

Kenneth Dyar and Bert Blaauw, who are now independent investigators, generated in my lab muscle-specific and inducible knockouts of *Bmal1*, a master circadian gene. The most important result of this study has been the demonstration that the intrinsic muscle clock controls muscle insulin sensitivity and muscle metabolism (*Mol Metab* 2013).

Dyar KA, ... Blaauw B, Schiaffino S, Uhlenhaut NH (2018) Transcriptional programming of lipid and amino acid metabolism by the skeletal muscle circadian clock. *PLoS Biol*, 16:e2005886.

Dyar KA, ... Schiaffino S, Blaauw B (2015) The calcineurin-NFAT pathway controls activity-dependent circadian gene expression in slow skeletal muscle. *Mol Metab*, 4:823-33.

Dyar KA, ... Blaauw B, **Schiaffino S** (2013) Muscle insulin sensitivity and glucose metabolism are controlled by the intrinsic muscle clock. *Mol Metab*, 3:29-41.

The role of the MRF4-MEF2 axis in the control of muscle growth

We found that a member of the MyoD family of myogenic regulatory factors, MRF4, coded by *MYF6*, controls muscle mass by repressing myocyte enhancer binding factor 2 (MEF2) activity in adult skeletal muscle (*Nat Commun*, 2016). This finding opens a new perspective for preventing muscle wasting.

Moretti I, ... **Schiaffino S** (2016) MRF4 negatively regulates muscle growth by repressing MEF2 activity. *Nat Commun*, 7:12397.

Single muscle fiber proteomics

In collaboration with Marta Murgia and Matthias Mann (Munich) we characterized the proteomic profile of the different fiber types in mouse (*EMBO Rep* 2015) and human skeletal muscle (*Cell Rep* 2017; *Skelet Muscle*, 2021). More recently, the changes in the protein profile induced by bed rest and spaceflight were also examined.

Murgia M, ... Schiaffino S, ... Mann M (2022) Signatures of muscle disuse in spaceflight and bed rest revealed by single muscle fiber proteomics. *PNAS Nexus*, 1:1-14.

Murgia M, ... **Mann M, Schiaffino S** (2021) Protein profile of fiber types in human skeletal muscle. A single-fiber proteomics study. *Skelet Muscle*, 11, 24.

Murgia M, ... Schiaffino S, Reggiani C, Mann M (2017) Single muscle fiber proteomics reveals fiber-type-specific features of human muscle aging. *Cell Rep*, 19: 2396-2409.

Murgia M, ... **Schiaffino S, Mann M** (2015) Single muscle fiber proteomics reveals unexpected mitochondrial specialization. *EMBO Rep*, 16: 387-395.

The human myotendinous junction (MTJ): proteomic profile and single-nucleus RNA-seq While I was visiting professor in Copenhagen in the lab of Abigail Mackey and Michael Kjaer, I promoted a collaboration with the lab of Matthias Mann (Novo Nordisk Foundation Center for Protein Research, Copenhagen) to analyze the human muscle-tendon junction by proteomics. This study led to the identification of novel MTJ protein markers. A single-nucleus RNA-sequencing (snRNA-seq) analysis has revealed the existence of subclusters of MTJ myonuclei with distinct gene expression profiles.

Karlsen A, ... Schiaffino S, Kjaer M, Mackey LA (2023) Distinct myofibre domains of the human myotendinous junction revealed by single nucleus RNA-seq. *J Cell Sci*, 136:jcs.260913.

Karlsen A, ... Schiaffino S, Mackey A, Deshmukh AS (2022) The proteomic profile of the human myotendinous junction. *iScience*, 25(2),103836.

Reviews & Editorials (selected)

Schiaffino S, Chemello F, Reggiani C (2024) The diversity of muscle fiber types. *Cold Spring Harbor Perspect Biol*, Aug 12:a041477. Online ahead of print. doi: 10.1101/cshperspect.a041477.

Franco-Romero A, **Sandri M, Schiaffino S** (2024) Autophagy in skeletal muscle. *Cold Spring Harbor Perspectives in Biology*. Aug 12:a041565. doi: 10.1101/cshperspect.a041565. Online ahead of print.

Schiaffino S, Hughes SM, Murgia M, Reggiani C (2024) MYH13, a superfast myosin expressed in extraocular, laryngeal and syringeal muscles. *J Physiol*, 602:427-443.

Schiaffino S, Reggiani C, Akimoto T, Blaauw B (2021) Molecular mechanisms of skeletal muscle hypertrophy. *J Neuromuscular Dis*, 8:169-183.

Schiaffino S (2017) Losing pieces without disintegrating: Contractile protein loss during muscle atrophy. *Proc Natl Acad Sci USA*, 114:1753-55.

Schiaffino S, Rossi AC, Smerdu V, Leinwand LA, Reggiani C (2015) Developmental myosins: expression patterns and functional significance. *Skelet Muscle*, 5:22.

Schiaffino S, Dyar KA, Ciciliot S, Blaauw B, **Sandri M** (2013) Mechanisms regulating skeletal muscle growth and atrophy. *FEBS J*, 280:4294-4314.

Ciciliot S, Rossi AC, Dyar KA, Blaauw B, **Schiaffino S**. Muscle type and fiber type specificity in muscle wasting (2013) *Int J Biochem Cell Biol*, 45:2191-9.

Blaauw B, Schiaffino S, Reggiani C. (2013) Mechanisms modulating skeletal muscle phenotype. *Compr Physiol* 3: 1645-87.

- Schiaffino S** (2012) Tubular aggregates in skeletal muscle: Just a special type of protein aggregates? *Neuromuscul Disord*, 22:199-207.
- Schiaffino S**, Mammucari C (2011) Regulation of skeletal muscle growth by the IGF1-Akt/PKB pathway: insights from genetic models. *Skelet Muscle*, 1:4.
- Schiaffino S**, Reggiani C (2011) Fiber types in mammalian skeletal muscle. *Physiol Rev*, 91:1447-1531.

Invited speaker (selected)

- 2024 Institute of Biochemistry, University of Cologne, Oct 2024
- 2023 Bureš Lecture, Institute of Physiology of the Czech Academy of Sciences, Prague, Oct 2023.
- 2023 Keynote Lecture, 1st Symposium Lyon-Lausanne-Padua", Padova, April 2023.
- 2023 Società Italiana dell'Obesità, Padova, Jan 2023.
- 2022 National Center of Neurology and Psychiatry (NCNP), Tokyo, Oct 2022.
- 2022 Keynote Lecture, European Muscle Conference, Prague, Sept 2022.
- 2022 Keynote Lecture, 2022 Padua Days of Muscle & Mobility Medicine, March 2022.
- 2020 Keynote Lecture, 12th Munich Muscle Meeting (MMM), Dec 2020.
- 2019 Keynote Lecture, Symposium of Clinical Academic Group on Exercise, Copenhagen, Nov 2019.
- 2019 Seminar, Institut Cochin, Paris, March 2019.
- 2019 2nd Workshop "Skeletal muscle research - from cell to human", Ljubljana (Slovenia), May 2019.
- 2019 Meeting in honor of Gillian Butler-Browne, Institut de Myologie, Paris, March 2019.
- 2018 August Krogh Club Seminar, Copenhagen, Oct 2018.
- 2018 Symposium in honor of Carlo Reggiani, Padova, Oct 2018.
- 2018 Keynote Lecture, Conference on "Exercise and musculoskeletal system", Lyon, May 2018.
- 2018 Giovanni Salviati Memorial Meeting, Padova, March 2018.
- 2017 Closing remarks, Copenhagen Bioscience Conferences, Hillerød, Oct 2017.
- 2017 Keynote lecture, Gordon Research Conference on Myogenesis, Il Ciocco (Lucca), June 2017.
- 2017 Workshop "Skeletal muscle research - from cell to human", Ljubljana (Slovenia), May 2017.
- 2017 Conference on "Advances in Skeletal Muscle Biology, Gainesville, FL, March 2017.
- 2016 Symposium on "Targeting skeletal muscle oxidative metabolism", London, Oct 2016.
- 2016 ECTS 2016, 43rd Congress of the European Calcified Tissue Society, Rome May 2016.
- 2016 Workshop on Musculoskeletal Ageing (CIMA), Manchester May 2016.
- 2016 Congress on "Muscle decline in aging", Terme Euganee (Padova) Apr 2016.
- 2015 "The Saltin Symposium. Exercise and Integrative Physiology", Copenhagen, June 2015.
- 2015 Karolinska Institutet, Stockholm.
- 2014 University of Copenhagen.
- 2014 EMBO Conference "Molecular Biology of Muscle Development", Acaya-Lecce.
- 2013 August Krogh Symposium, Copenhagen, Nov 2013.
- 2013 Symposium "Muscle and matrix", Borupgaard, Snekkersten (Denmark).
- 2012 Conference on "The Biomedical Basis of Elite Performance", London.
- 2012 MYOAGE Symposium on "The aging human muscle", Copenhagen.
- 2012 Keynote lecture, European Muscle Conference, Rhodes (Greece).
- 2011 German Physiological Society, Regensburg.
- 2011 International Conference "Amino Acid/Protein Metabolism", Santa Margherita Ligure (Genova).
- 2011 EMBO Congress "Skeletal muscle development and regeneration", Wiesbaden.
- 2011 University of Colorado Boulder, Aug 2011.
- 2011 Conference "Molecular mechanisms of skeletal muscle wasting and repair", Ascona.

Organization of Meetings

- 2016 Symposium on "Bone & Muscle", European Calcified Tissue Society (ECTS), Roma.
- 2014 Golgi meeting "La comunicazione tra cellule neuronali", Accademia dei Lincei, Roma.
- 2011 5th National Congress of the Italian Society for Space Biomedicine, Padova.
- 2011 Workshop "The mammalian circadian clock", Padova, Apr 2011.

Lectures to PhD and Master students, member of thesis committees

- 2022 Lecture to PhD students, Waseda University, Tokorozawa (Japan).
- 2019 PhD thesis of Manuel Dos Santos, Université Paris Descartes, Paris
- 2016 Summer School PhD course "Biomedicine", Padova
- 2013 SummerSchool on "Basic Muscle Sciences", Max-Delbrück-Centre for Molecular Medicine, Berlin
- 2013 PhD thesis of Marie Victoire Neguebor, Università Vita Salute San Raffaele, Milano
- 2012 Workshop Marie Curie ITN program MUZIC, Padova

- 2012 PhD Thesis of Ricardo José Ribeiro Soares, University of Coimbra, Portugal
 2012 Cell Biology Master Course 2012-2013, Sorbonne Universités, UPMC, Paris

Advisory boards and committees

- 2023-27 10th Scientific Council, Commission “Fundamental Myology”, AFM-Téléthon, Paris.
 2023 Council for Medical Sciences, Independent Research Fund Denmark, Copenhagen.
 2020-22 9th Scientific Council, Commission “Fundamental Myology”, AFM-Téléthon, Paris.
 2018 Committee for selection of group leaders at GReD, Clermont-Ferrand (France).
 2017-18 Council for Medical Sciences, Independent Research Fund Denmark, Copenhagen.
 2016-18 Member of the jury for the selection of candidates, Institut Universitaire de France.
 2016 Italian National Agency for the Evaluation of Universities and Research Institutes (ANVUR).
 2017 “Bedrest Announcement of Opportunity”, ESA and NASA (Washington).
 2017-19 8th Scientific Council, Commission “Fundamental Myology”, AFM-Téléthon, Paris.
 2015-16 Coordinator of the Italian Space Agency working group on “Biomedicine and Life Sciences”.
 2014-19 Scientific Council, Stazione Zoologica Anton Dohrn, Naples.
 2014-19 Scientific Advisory Board, “Institut Neuro-Myo-Gène”, Lyon.
 2014-16 7th Scientific Council, Commission “Fundamental Myology”, AFM-Téléthon, Paris.
 2014 Musculoskeletal Panel, ILSRA (International Life Science Research Announcement), Experiments in the International Space Station (NASA, ESA, JAXA and CSA), Washington.
 2013-14 European Space Agency (ESA) projects on “Bed Rest” and “Concordia Station (Antarctic)”.
 2013-14 Selection Committee, Pathophysiology, Agence Nationale de la Recherche (ANR), Paris
 2011-13 6th Scientific Council, Commission “Fundamental Myology”, AFM-Téléthon, Paris.
 2011-12 Council for Medical Sciences, Independent Research Fund Denmark, Copenhagen.

Ad hoc reviewer, consultant

- Grants: ERC, ESF, Wellcome Trust, ANR (Agence Nationale de la Recherche) ...
- Articles: Nature Med, Nature Cell Biol, Nature Commun, Sci Adv, PNAS, J Clin Invest, J Cell Biol, ...
- Candidates for fellowships & positions: Royal Society, Australian Academy of Science, ...
- Consultancy: Consultant, Clinical trial phase 2 (drug for treatment for DMD), Summit (Oxford) Ltd.

Visiting scientists in my lab

- Sammy Wing-Sum Siu, Research Associate, Chinese University of Hong Kong (July 2018).
- Tatiana Y. Kostrominova, Associate Professor, Indiana University, USA (April-June 2015).
- Nobuko Hagiwara, Associate Professor, UC Davis School of Medicine, Davis, CA, USA (Sept 2011).
- Takayuki Akimoto, Assistant Professor, Faculty of Medicine, University of Tokyo (2010-11).

Grants, Fellowships

EC VII Program project “MYOAGE” (2009-14); Marie Curie ITN program “MUZIC” (2010-13); AFM-Téléthon (2013-15). Fellowship by the Japan Society for the Promotion of Science (2021).

Alumni (recent)

- Bert Blaauw is now Professor of Physiology, Department of Biomedical Sciences, University of Padova.
- Kenneth A. Dyar is now Group leader and Head of the Division for Metabolic Physiology, Institute for Diabetes and Cancer, Helmholtz Zentrum München.

Accademia dei Lincei

As a member of the Accademia dei Lincei, and of the Lincei committees on Health and on COVID-19, I have been involved in the activities of the Accademia aimed at increasing public understanding of COVID-19 and providing objective advice to the Italian government on this matter. In addition to several documents and statements, we published some papers on COVID-19:

- Forni et al, COVID-19 vaccines: where we stand and challenges ahead. Cell Death Differ, 28:626-639, 2021.
- Mantovani et al, Long COVID: where we stand and challenges ahead. Cell Death Differ, 29:1891-1900, 2022.
- Remuzzi et al, Drugs for the prevention and treatment of COVID-19 and its complications: An update on what we learned in the past two years. Front Pharmacol, 13, 987816, 2022.

2021 Committee for the G20 Science (S20) on “Pandemic preparedness”

2023 Committee of the Lincei meeting on “Cell signalling: a meeting in memory of Tullio Pozzan”

2024 Steering committee Meeting of Lincei with the UK Academy of Medical Sciences on “Child Obesity”

2025 Course of the Foundation “I Lincei per la Scuola” on “Correct Styles of Life”.