SILVIA BRUNELLI
Date and place of birth: December 30th 1969, Milano.

Associate Professor, School of Medicine and Surgery, University of Milano-Bicocca, Milano Italy

EDUCATION
BsC cum laude: December 11, 1993, Faculty of Biology, University of Milano.
PhD in cellular and molecular biology: March 28, 1998, Open University, London / DIBIT Milano.

AWARDS
2014: Abilitazione Nazionale for Associate Professorship in: Developmental biology (05/B2), Histology (05/H2), Molecular biology (05/E2), Applied Biology (05/F1),
2014: Abilitazione Nazionale for Full Professorship in: Applied Biology (05/F1).
1998: Marie Curie Training Network IF fellowship (postgraduate)
1997: Marie Curie Training Network IF fellowship (undergraduate)

RESEARCH TRAINING AND EXPERIENCE
Employment and research experience
-1994-1997: PhD student (Open University-UK) In the lab of Prof Edoardo Boncinelli, at DIBIT-HSR, Milano. During this period she has identified EMX2 as a critical gene in the normal and abnormal development of the cerebral cortex with a correlation to the schizencephaly disease.
-August 1997-April 1999: EC fellow in the laboratory of Dr. Robin Lovell-Badge, NIMR, London, UK.
-April 1999-March 2001 MRC research associate in the laboratory of Dr. Robin Lovell-Badge, NIMR, London, UK. In these years, she first focused on studying he role of HMG containing transcription Sox3 gene in gastrulation and in the development of central nervous system.
-March 2001-January 2005: Postdoc scientist in the laboratory of Prof. Giulio Cossu, S.C.R.I., DIBIT-HSR, Milan, Italy. In those years she has focused on the myogenic differentiation mechanism of mesoangioblast stem cells in vivo and in vitro, and she has studied the molecular mechanisms leading to myogenesis in the embryo, identifying a new Wnt non-canonical pathway linking Pax3 to the the dorsal ecdoderm-driven myogenesis. She has identified for the first time a novel gene, necdin, involved in the fate choice of mesoangioblasts and in the regenerative process in the skeletal muscle, a line of research that has been financed by Telethon. In this period she has established a fruitful collaboration with Dr. Margaret Buckingham, at the Pasteur Institute, Paris.
-February 2005-March 2015: Assistant Professor, Dept. Experimental Medicine (now Department of Health Sciences) University of Milano-Bicocca, Milano. She has started her independent career focusing on molecular biology of development and stem cells, muscle regeneration and differentiation in physiological and pathological conditions, in particular in the muscular dystrophies.
- 2008-2015 she is also Group Leader of the unit of Functional Genetics of Muscle Regeneration, in the Division of Regenerative Medicine, Stem Cells and Gene Therapy, DIBIT, San Raffaele Scientific Institute.
In collaboration with Prof. Giulio Cossu and Prof. Emilio Clementi, she has contributed to the identification of a new role for nitric oxide and later of mitochondria dynamics in myogenic differentiation, that has opened the field to new therapeutic strategies to muscle dystrophy, combining pharmacological and stem cell approaches. This expertise is critical for the development of theraputic strategies in the present proposal. She has also started a collaboration with Dr. Patrizia Rovere-

Querini at Dibit San Raffaele; by combining the immunological expertise of Dr. Rovere-Querini, with her own experience in muscle biology and stem cells, they have started a fruitful interaction that has opened a new line of research on how the native immunity influences muscle repair. In parallel she has established a line of research on the identification and activation of vessel associated progenitor in development and in muscle regeneration and neoangiogenesis, and the cross talk between innate immunity and the endothelial mesenchymal transition in the onset and progression of musculoskeletal disorders. She has an ongoing collaboration with Dr. Gabriella Minchiotti at IGB-Naples, on the role of Cripto in muscle regenreration.
-from April 2015: Associate Professor in Cell Biology, in the Department of Health Sciences, University of Milano Bicocca.

--from 2015 she is member of the Istituto Nazionale Biostrutture e Biosistemi-Consorzio Interuniversitario

The large majority of the research activity performed by S. B. has been dedicated to muscle development and physiopathology, focusing on muscle-specific signalling pathways and gene expression and has led to acquire and develop essential tools, reagents and expertise to perform, an in-depth study of muscle differentiation, maintenance and regeneration. SB has also collaborated to the development of experimental therapeutic strategies to muscle degenerative disorders, in particular muscle dystrophy, combining pharmacological and stem cell approaches, and she has acquired experience in the experimental planning of new drugs and biopharma testing in animal models.

Funding

Fondazione Cariplo Ricerca Medica **2013** Role of cripto in orchestrating tissue remodelling in muscle damage
Coordinator of the project (2 units) and Unit PI

Italian Ministry of University PRIN **2012** Identificazione di nuove molecole terapeutiche per le malattie muscolari orfane su base infiammatoria
Unit PI

FP7-Health **2010** Endostem (241440): Activation of vasculature associated stem cells and muscle stem cells for the repair and maintenance of muscle tissue
Workpackage leader (6 units) and Unit PI

Association Française contre les Myopathies AFM **2009**: The role of iron handling by macrophages in the repair of muscle damage: relevance to muscle disorders
Project Coordinator (3 units) and Unit PI

Italian Ministry of University PRIN **2008**: Controllo del potenziale rigenerativo del muscolo scheletrico da parte di fattori che influenzino l'attivazione e il reclutamento di cellule staminali.
Unit PI

Italian Ministry of Health -Ricerca Finalizzata **2008:** Optimization of pre-clinical models of cell therapy for muscular dystrophy
Unit PI

Telethon **2007** GPGGP07013: Role of necdin in the differentiation and regeneration of the skeletal muscle:mechanism of action and application to the cell therapy of muscular dystrophy
PI (Single unit)

Fondazione Cariplo Ricerca Medica **2007**: Ottimizzazione di un protocollo di terapia cellulare per la Distrofia Muscolare di Duchenne
Unit PI

Fondazione Cariplo Ricerca Medica **2007**: Eterogeneità genetica nella sclerosi laterale amiotrofica ad esordio giovanile: meccanismi molecolari di degenerazione neuronale e muscolare, approccio di genomica e proteomic per l' identificazione di nuovi geni per la diagnostica delle malattie del motoneurone
Unit PI

Italian Ministry of Health Progetto ex art 56 anno **2006:** Malattia del motoneurone: pathway molecolari e cellulari nella degenerazione neuronale e muscolare come causa di eterogeneita' clinica e genetica
Unit PI

Editorial activity
She is member of the editorial board of “Stem Cells International” and “Fronteers in Immunology”

Others
She has been invited to give seminars in several national and international research institutes and universities. She has been invited speaker in international and national meetings organized by; Associazione di Biologia Cellulare e del Differenziamento; the American Society for Cell Biology; the British Society for Developmental Biology: the International Society of in vivo Toxicology; FASEB Myogenesis.

Patents
Bianchi ME, Vénéreau EJ, Casalgrandi M, Brunelli S (2013). HMGB1 Variants and Uses thereof. US Provisional n. 61/676,071; PCT/EP2013/065829

Cossu G, Clementi E, Brunelli S (2007). Method of treatment for muscular dystrophy. WO2007088050 - 2007-08-09.

Clementi E, Cossu G, Brunelli S, Ongini E (2007). Use of nitrooxyderivative of drug for the treatment of muscular dystrophies. WO2007088123 - 2007-08-09

PUBLICATION AND SCORES
SB is author of 60 publications on peer-reviewed international journals indexed in Pubmed
H-index (Scopus): 26

PUBLICATIONS 2011-2016

1. Nicolosi PA, Tombetti E, Maugeri N, Rovere-Querini P, Brunelli S and Manfredi AA (2016) Vascular Remodelling and Mesenchymal Transition in Systemic.doi.org/10.1155/2016/4636859

2. Valentina Conti, Anna Gandaglia, Francesco Galli, Mario Tirone, Elisa Bellini, Lara Campana, Charlotte Kilstrup-Nielsen, Patrizia Rovere-Querini, Silvia Brunelli, and Nicoletta Landsberger. (2015) MeCP2 Affects Skeletal Muscle Growth and Morphology through Non Cell-Autonomous Mechanisms. *PLoS ONE* 10:e0130183.
3. Touvier T, De Palma C, Rigamonti E, Scagliola A, Incerti E, Mazelin L, Thomas JL, D'Antonio M, Politi L, Schaeffer L, Clementi E, Brunelli S. Muscle-specific Drp1 overexpression impairs skeletal muscle growth via translational attenuation. Cell Death Dis. 2015 Feb 26;6: e1663. doi: 10.1038/cddis.2014.595
4. Dentice M, Ambrosio R, Damiano V, Sibilio A, Luongo C, Guardiola O, Yennek S, Zordan P, Minchiotti G, Colao A, Marsili A, Brunelli S, Del Vecchio L, Larsen PR, Tajbakhsh S, Salvatore D. Intracellular inactivation of thyroid hormone is a survival mechanism for muscle stem cell proliferation and lineage progression. Cell Metab. 2014 Dec 2;20(6):1038-48
5. Azzoni E, Conti V, Campana L, Dellavalle A, Adams RH, Cossu G and Brunelli S. Hemogenic endothelium generates mesoangioblasts that contribute to several mesodermal lineages in vivo (2014). Development 141:1821-1834;
6. Bosurgi L., Brunelli S, Rigamonti E, Monno A, Manfredi A, Rovere-Querini P. Vessel-associated myogenic precursors control macrophage activation and clearance of apoptotic cells. (2014) Clinical and Experimental Immunology. Apr 21. doi: 10.1111/cei.12356.
7. Rigamonti E, Zordan P. Sciorati C, Rovere-Querini P and Brunelli S. Macrophage plasticity in skeletal muscle repair (2014). BioMed Research International. Vol 2014. http://dx.doi.org/10.1155/2014/560629
8. Venturin M, Carra S, Gaudenzi G, Brunelli S, Gallo GR, Moncini S, Cotelli F, Riva P. ADAP2 in heart development: a candidate gene for the occurrence of Cardiovascular Malformations in NF1 Microdeletion Syndrome (2014). Journal of Medical Genetics. doi: 10.1136/jmedgenet-2013-102240
9. Zordan, P, Rigamonti, E, Freudenberg, K, Conti, V, Azzoni, E, Patrizia Rovere-Querini, P, Brunelli, S. Macrophages commit postnatal endothelium derived-progenitors to angiogenesis and restrict endothelial to mesenchymal transition during muscle regeneration. (2014). Cell Death and Disease. Jan 30;5:e1031
10. Rovere-Querini, P, Clementi, E, Brunelli, S. Nitric Oxide and muscle repair: multiple actions converging on therapeutic efficacy (2013). European Journal of Pharmachology. 730:181-5.
11. Cazzato. D, Assi, E, Moscheni, C, Brunelli, S, De Palma, S, Cervia, D, Perrotta, C, Clementi, E. Nitric Oxide drives embryonic myogenesis in chicken through the upregulation of myogenic differentiation factors (2013). Experimental Cell Research. 320(2):269-80
12. D'Orlando, C, Marzetti, E, François S, Lorenzi M, Conti V, Di Stasio E, Rosa F, Md, Brunelli S, Doglietto Gb, Pacelli F, Bossola M. Gastric cancer does not affect the expression of atrophy-related genes in human skeletal muscle. (2013). Muscle Nerve Jul 8. 49(4):528-33
13. Dormoy-Raclet, V, Cammas A, Celona B, Lian Xl, Van Der Giessen K, Zivojnovic M, Brunelli S, Riuzzi F, Sorci G, Wilhelm G, Di Marco S, Donato R, Bianchi Me, Imed-Eddine Gallouzi I-E. (2013). HuR and miR-1192 regulate myogenesis by modulating the translation of HMGB1 mRNA. Nature Communications. 4:2388
14. Zordan P, Sciorati C, Campana L, Cottone L, Clementi E, Rovere-Querini P, Brunelli S. The Nitric Oxide-donor molsidomine modulates the innate inflammatory response in a mouse model of muscular dystrophy (2013). European Journal of Pharmachology 715(1-3):296-303
15. Rigamonti E, Touvier T, Clementi E, Manfredi A, Brunelli S, Rovere-Querini P. Requirement of inducible Nitric Oxide Synthase for skeletal muscle regeneration after acute damage. Journal of Immunology (2013). 190(4):1767-77.

16. Guardiola O, Lafuste P, Brunelli S, Iaconis S, Touvier T, Mourikis P, De Bock K, Lonardo E, Andolfi G, Bouché A, Liguori Gl, Shen Mm Tajbakhsh S, Cossu G, Carmeliet P, Minchiotti G. Cripto regulates skeletal muscle regeneration and modulates satellite cell determination by antagonizing Myostatin. Proc Natl Acad Sci U S A. (2012) 109(47):E3231-40. doi: 10.1073/pnas.1204017109. Epub 2012 Nov 5.
17. François S, D'Orlando C, Fatone T, Touvier T, Pessina P, Meneveri R, Brunelli S. Necdin enhances myoblasts survival by facilitating the degradation of the mediator of apoptosis CCAR1/CARP1. PLoS One. (2012);7(8):e43335.
18. D'Angelo MG, Gandossini S, Martinelli Boneschi F, Sciorati S, Bonato B, Brighina E, Comi Gp, Turconi Ac, Magri F, Stefanoni G, Brunelli S, Bresolin N, Cattaneo D, Clementi E. (2012). Nitric oxide donor and non steroidal anti inflammatory drugs as a therapy for muscular dystrophies: evidence from a safety study with pilot efficacy measures in adult dystrophic patients. Pharmacol Res. (2012) Apr;65(4):472-9. Epub 2012 Jan 25.
19. Bosurgi L, Corna G, Vezzoli M, Touvier T, Cossu G, Manfredi Aa, Brunelli S, Rovere-Querini P. Transplanted mesoangioblasts require macrophage IL-10 for survival in a mouse model of muscle injury. J Immunol. 2012 Jun15;188 (12):6267-77. Epub 2012 May 9.
20. Buono R, Vantaggiato C, Pisa V, Azzoni E, Bassi Mt, Brunelli S, Sciorati C, Clementi E. Nitric oxide sustains long-term skeletal muscle regeneration by regulating fate of satellite cells via signaling pathways requiring Vangl2 and cyclic GMP. Stem Cells. (2012) Feb;30(2):197-209
21. Pessina P, Conti V, Tonlorenzi R, Touvier T, Meneveri R, Cossu G, Brunelli S. (2011). Necdin enhances muscle reconstitution of dystrophic muscle by vessel associated progenitors, by promoting cell survival and myogenic differentiation. Cell Death And Differentiation. 19(5):827-38
22. Dellavalle A, Maroli G, Covarello D Azzoni E, Innocenzi A, Perani L, Antonini S, Sambasivan R, Brunelli S, Tajbakhsh S, Cossu G. (2011). Pericytes resident in postnatal skeletal muscle differentiate into muscle fibres and generate satellite cells. Nature Communications. 2:499
23. Donati C, Marseglia G, Magi A, Serratì S, Cencetti F, Bernacchioni C, Nannetti G, Benelli M, Brunelli S., Torricelli F, Cossu G, Bruni P (2011). Sphingosine 1-Phosphate Induces Differentiation of Mesoangioblasts towards Smooth Muscle. A Role for GATA6. Plos One, vol. 6; p. e20389.
24. Sciorati C, Miglietta D, Buono R, Pisa V, Cattaneo D, Azzoni E, Brunelli S., Clementi E (2011). A dual acting compound releasing nitric oxide (NO) and ibuprofen, NCX 320, shows significant therapeutic effects in a mouse model of muscular dystrophy. Pharmacological Research, 64(3): 210-7.
25. Vezzoli M, Castellani P, Corna G, Castiglioni A, Bosurgi L, Monno A, Brunelli S., MANFREDI AA, RUBARTELLI A, ROVERE-QUERINI P (2011). HMGB1 release and redox regulation accompany regeneration and remodeling of skeletal muscle. Antioxidants & Redox Signaling,15(8):2161-74

ORCID CODE