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## BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE		
Rudnicki, Michael Anthony	Senior Scientist and Director, Regenerative Medicine Program, Ottawa Health Research Institute		
eRA COMMONS USER NAME			
MRUDNICKI@OHRI.CA			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University of Ottawa, Canada	B.Sc.	1982	Molecular Biology
University of Ottawa, Canada	Ph.D.	1988	Biology
Whitehead Institute, Cambridge, MA	PDF	1992	Molecular Genetics

### A. Positions and Honors.

#### Positions and Employment

1982-88: Graduate student (advisor: Dr. Michael McBurney), University of Ottawa Canada  
1988-92: Postdoctoral fellow (advisor: Dr. Rudolf Jaenisch), Whitehead Institute, MIT, Cambridge, MA.  
1992-97: Assistant Professor, Department of Pathology, McMaster University, Canada.  
1997-2000: Associate Professor, Department of Pathology, McMaster University, Canada.  
1999-2004 Medical Research Council of Canada, Research Scientist Award  
2000-present Senior Scientist, Ottawa Health Research Institute  
2000-present Director, Program in Regenerative Medicine, Ottawa Health Research Institute  
2000-present Professor, Department of Medicine, University of Ottawa  
2004-present Scientific Director, Canadian Stem Cell Network

#### Other Experience and Professional Memberships

1995-1998 Medical Research Council, Genetics Panel  
1996 National Institutes of Health, Ad Hoc member, Biology II Study Section  
1997 National Institutes of Health, Ad Hoc member, Mammalian Genetics  
1998-2001 Chair of Genetics, Medical Research Council  
1998 MRC Genomics Special Projects, Letters of Intent Review Committee  
1999-2004 Muscular Dystrophy Association (USA), Scientific Advisory Committee  
2001-present College of Reviewers, Canada Research Chairs Program  
2001: NIH study section, NSD-C Review Committee, Ad Hoc Member.  
2001-2005 Standing Committee on Oversight of Grants and Awards Competitions, CIHR  
2002-2006 Deutsche Forschungsgemeinschaft Stem Cells Review Panel  
2004-present International Society of Differentiation, Member Board of Directors  
2004-present Editorial Board Member "Journal of Cell Biology"  
2005-2006 European Commission, 6th Framework Genomics Review Panel  
2005-2008 The Gairdner Foundation Medical Review Panel  
2005-present Scientific Director, Canadian Stem Cell Network  
2006-present Editorial Board Member "Cell Stem Cell"  
2008-present Scientific Director, International Regulome Consortium

#### Honors

1985-987 National Cancer Institute of Canada Studentship.  
1988-1991 National Cancer Institute of Canada Junior Post-doctoral Fellowship.  
1993-1999 National Cancer Institute of Canada Research Scientist Award  
1999-2004 Medical Research Council of Canada, Research Scientist Award  
1999-2004 Premier's Research Excellence Award, Province of Ontario  
2001-2008 Canada Research Chair in Molecular Genetics (Tier 1)  
2002-2007 Howard Hughes Medical Institute Research International Scholar  
2006-present Fellow of the Royal Society of Canada  
2007-2012 Howard Hughes Medical Institute International Research Scholar  
2009-2016 Canada Research Chair in Molecular Genetics (Tier 1)

## B. Selected peer-reviewed publications (in chronological order).

(Publications selected from 143 peer-reviewed publications)

1. Rudnicki, M.A., Braun, T., Hinuma, S., and Jaenisch, R. (1992). Inactivation of MyoD in mice leads to up-regulation of the myogenic HLH gene Myf-5 and results in apparently normal muscle development. *Cell* 71: 383-390.
2. Braun, T., Rudnicki, M.A., Arnold, H.H., and Jaenisch, R. (1992). Targeted inactivation of the muscle regulatory gene Myf-5 results in abnormal rib development and perinatal death. *Cell* 71: 369-382.
3. Mombaerts, P., Clarke, A.R., Rudnicki, M.A., Iacomini, J., Itohara, S., Lafaille, J.J., Wang, L., Ichikawa, Y., Jaenisch, R., Hooper, M.L., and Tonegawa, S. (1992). Mutations in T-cell antigen receptor genes a and b block thymocyte development at different stages. *Nature* 360: 225-231.
4. Rudnicki, M.A., Schnegelsberg, P.N.J., Stead, R.H., Braun, T., Arnold, H.H., and Jaenisch, R. (1993). MyoD or Myf-5 is required for the formation of skeletal muscle. *Cell* 75: 1351-1359.
5. LeCouter, J.E., Whyte, P.F.M., and Rudnicki, M.A. (1996). Cloning and expression of the Rb-related mouse p130 mRNA. *Oncogene* 12: 1433-1440.
6. Megeney, L.A., Kablar, B., Garrett, K., Anderson, J.E., and Rudnicki, M.A. (1996). MyoD is required for myogenic stem cell function in adult skeletal muscle. *Genes Dev.* 10: 1173-1183.
7. Megeney, L.A., Perry, R., LeCouter, J.E., and Rudnicki, M.A. (1996). bFGF and LIF signaling activates STAT3 in proliferating myoblasts. *Dev. Gen.* 19: 139-145.
8. Kablar, B., Krastel, K., Ying, C., Asakura, A., Tapscott, S.J., and Rudnicki, M.A. (1997). MyoD and Myf-5 differentially regulate the development of limb versus trunk skeletal muscle. *Development* 124: 4729-4738.
9. LeCouter, J.E., Kablar, B., Whyte, P.F.M., Ying, C., and Rudnicki, M.A. (1998). Strain-dependent embryonic lethality in mice lacking the retinoblastoma-related p130 gene. *Development* 125: 4669-4679.
10. LeCouter, J.E., Kablar, B., Hardy, W.R., Ying, C., Megeney, L.A., May, L.L., and Rudnicki, M.A. (1998). Strain-dependent myeloid metaplasia, growth deficiency, and shortened cell-cycle in mice lacking p107. *Mol. Cell. Biol.* 18: 7455-7465.
11. Megeney, L.A., Kablar, B., Perry, R.L.S., Ying, C., May, L.L., and Rudnicki, M.A. (1999). Severe cardiomyopathy in mice lacking dystrophin and MyoD. *Proc. Nat'l. Acad. Sci. USA* 96: 220-225.
12. Kablar, B., Krastel, K., Ying, C., Tapscott, S.J., Goldhamer, D.J. and Rudnicki, M.A. (1999). Myogenic determination occurs independently in somites and limb buds. *Dev. Biol.* 206: 216-231.
13. Sabourin, L.A., Girgis-Gabardo, A., Seale, P., Asakura, A., and Rudnicki, M.A. (1999). Reduced differentiation potential of primary MyoD<sup>-/-</sup> myogenic cells derived from adult skeletal muscle. *J. Cell Biol.* 144: 631-643.
14. Kablar, B., and Rudnicki, M.A. (1999). Development in the absence of skeletal muscle results in the sequential ablation of motor neurons from the spinal cord to the brain. *Dev. Biol.* 208: 93-109.
15. Kablar, B., Asakura, A., Krastel, K., Ying, C., May, L., Goldhamer, D.J. and Rudnicki, M.A. (1999). MyoD and Myf-5 define the specification of musculature of distinct embryonic origin. *Biochem. Cell Biol.* 76: 1079-1091.
16. Sabourin, L.A., and Rudnicki, M.A. (1999). Induction of apoptosis by SLK, a Ste20-related kinase. *Oncogene* 18: 7566-7575.
17. Sabourin, L.A., Seale, P., Wagner, J., and Rudnicki, M.A. (2000). Caspase-3 cleavage of the Ste20-related kinase SLK releases and activates an apoptosis-inducing kinase domain and an actin disassembling region. *Mol. Cell. Biol.* 20: 684-696.
18. Kablar, B., Tajbakhsh, S., and Rudnicki, M.A. (2000). Transdifferentiation of esophageal smooth to skeletal muscle is myogenic bHLH factor dependent. *Development* 127: 1627-1639.
19. Seale, P., Sabourin, L.A., Girgis-Gabardo, A., Mansouri, A., Gruss, P., and Rudnicki, M.A. (2000). Pax7 is required for the specification of myogenic satellite cells. *Cell* 102: 777-786.
20. Perry, R.L.S., Parker, M., and Rudnicki, M.A. (2001). Activated MEK1 binds the MyoD transcriptional complex to repress transactivation. *Molecular Cell* 8: 291-301.
21. Asakura, A., Seale, P., Komaki, M. and Rudnicki, M.A. (2001). Muscle satellite cells are multipotential stem cells that differentiate into myocytes, adipocytes and osteocytes. *Differentiation* 68: 245-253.
22. Bergstrom, D.A., Penn, B.H., Strand, A., Perry, R.L.S., Rudnicki, M.A., and Tapscott, S.J. (2002). Promoter specific regulation of MyoD binding and signal transduction cooperate to pattern gene expression. *Molecular Cell* 9:587-600.
23. Asakura, A., Seale, P., Motohiro Komaki, M., Girgis-Gabardo, A., and Rudnicki, M.A. (2002). Myogenic specification of side population cells in skeletal muscle. *J. Cell Biol.* 159:123-134.
24. Asakura, A., and Rudnicki, M.A. (2002). Side population cells from diverse adult tissues are capable of in vitro hematopoietic differentiation. *Exp. Hematol.* 30:1339-1345.
25. Kablar, B., and Rudnicki, M.A. (2002). Information provided by the skeletal muscle and associated neurons is necessary for proper brain development. *Int. J. Dev. Neurosci.* 20:573-584.
26. Kablar, B., Krastel, K., Tajbakhsh, S. and Rudnicki, M.A. (2003). Myf5 and MyoD activation define independent myogenic compartments during embryonic development. *Developmental Biology* 258:307-

27. Polesskaya, A., Seale, P., and Rudnicki, M.A. (2003). Wnt signaling induces the myogenic specification of resident CD45+ adult stem cells during muscle regeneration. *Cell* 113:841-852.
28. Seale, P., Ishibashi, J., Scime, A., and Rudnicki, M.A. (2004). Pax7 is necessary and sufficient for the myogenic specification of CD45+/Sca1+ stem cells derived from injured muscle. *PLoS Biol.* 2(5):E130. Epub May 11.
29. Seale, P., Ishibashi, J., Holterman, C. and Rudnicki, M.A. (2004). Muscle satellite specific genes identified by genetic profiling of MyoD-deficient myogenic cells. *Developmental Biology* 275:287-300.
30. Huh, M.S., Parker, M.H., Scime, A. Parks, R., and Rudnicki, M.A. (2004). Rb is Required for Progression through Myogenic Differentiation but not Maintenance of Terminal Differentiation. *J. Cell Biol.* 166:865-876.
31. Ishibashi, J., Perry, R.L.S., Asakura, A. and Rudnicki, M.A. (2005). MyoD induces myogenic differentiation through cooperation of its N- and C-terminal regions. *J. Cell Biol.* 171: 471-482.
32. Scime, A., Grenier, G., Huh, M.S., Gillespie, M.A., Bevilacqua, L., Harper, M.E., and Rudnicki, M.A. (2005). Rb and p107 Regulate Preadipocyte Differentiation into White versus Brown Fat through Repression of PGC-1 $\alpha$ . *Cell Metabolism* 2:283-295.
33. Kuang, S. Charge, S.B., Seale, P., Huh, M., and Rudnicki, M.A. (2006). Distinct roles for Pax7 and Pax3 in adult regenerative myogenesis. *J. Cell Biol.* 172:103-113.
34. Parker, M.H., Perry, R.L.S., Fauteux, M.C., Berkes, C.A., and Rudnicki, M.A. (2006). MyoD synergizes with the E-Protein HEB $\beta$  to induce myogenic differentiation. *Mol. Cell. Biol.* 15:5771-5783.
35. Kuang, K., Kuroda, K., Le Grand, F., and Rudnicki, M.A. (2007). Asymmetric self-renewal and commitment of satellite stem cells in muscle. *Cell* 129(5):999-1010.
36. Campbell, P.A., Perez-Iratxeta, C., Andrade, M.A., and Rudnicki, M.A. (2007). Oct4 targets regulatory nodes to modulate stem cell function. *PLoS One* 2(6): e553. doi:10.1371.
37. McCann, J.A., Muro, E.M., Palmer, C., Palidwor, G., Porter, C.J., Andrade-Navarro, M.A., and Rudnicki, M.A. (2007). ChIP on SNP-chip for genome-wide analysis of human histone H4 hyperacetylation. *BMC Genomics* 8(1):322 [Epub ahead of print].
38. Asakura, A., Hirai, H., Kablar, B., Morita, S., Ishibashi, J., Piras, B.A., Christ, A.J., Verma, M., Vineretsky, K.A., and Rudnicki, M.A. (2007). Increased survival of muscle stem cells lacking the MyoD gene after transplantation into regenerating skeletal muscle. *Proc. Nat'l. Acad. Sci. (USA)* 104(42):16552-16557.
39. Holterman, C.E., Le Grand, F., Kuang, S., Seale, P., and Rudnicki, M.A. (2007). Megf10 regulates the progression of the satellite cell myogenic program. *Journal of Cell Biology* 179(5):911-922.
40. McKinnell, I.W., Ishibashi, J., Greenblatt, Le Grand, F., Punch, V.J.G., Addicks, G.C., Jack F Greenblatt, J.F., Dilworth, F.J., and Rudnicki, M.A. (2008). Pax7 activates myogenic genes by recruitment of a histone methyltransferase complex. *Nature Cell Biology* 10(1):77-84.
41. Seale, P., Bjork, B., Yang, W., Kajimura, S., Kuang, S., Scime, A., Devarakonda, S., Chin, S., Conroe, H., Rudnicki, M.A., Beier, D.R., and Spiegelman, B.M. (2008). PRDM16 controls a brown fat/skeletal muscle developmental switch. *Nature* 454(7207):961-967.
42. Le Grand, F., Scime, A., Jones, A.E., and Rudnicki, M.A. (2009). The planar cell Polarity pathway regulates the symmetric expansion of satellite stem cells. *Cell Stem Cell* 4(6):535-547.
43. 1. Abou-Khalil, R., Le Grand, F., Pallafacchina, G., Valable, S., Authier, F.-J., Rudnicki, M., Gherardi, R., Germain, S., Chretien, F., Sotiropoulos, A., Lafuste, P., Montarras, D., and Chazaud, B. (2009). Autocrine and paracrine Angiopoietin 1/Tie-2 signalling promotes muscle satellite cell self-renewal. *Cell Stem Cell* 5(3):298-309.
44. Gillespie, M.A., Le Grand, F., Scime, A, Kuang, S., von Maltzan, J., Seale, V., Cuenda, A., Ranish, J.A., and Rudnicki, M.A. (2009). p38 $\gamma$ -dependent gene silencing restricts entry into the myogenic differentiation program. *Journal of Cell Biology* 187(7):991-1005.
45. Joe, A.W., Natarajan, A., Le Grand, F., So, L., Wang, J., Rudnicki, M.A., and Rossi, F.M.V. (2010). Muscle injury activates resident fibro/adipogenic progenitors that facilitate myogenesis. *Nature Cell Biology* 12(2):153-163.

## C. Research Support

### Ongoing Research Support

R01 AR 44031-09A1 Rudnicki (PI) 04/01/2010 – 03/30/2015

NIH/NIAMS

Genetic Regulation of Skeletal Muscle Repair

The major goals of this project are to undertake a molecular analysis of Pax7 function and its post-translational regulation.

Role: PI

CIHR Rudnicki (PI)

10/01/2006 – 09/30/2011

Satellite Stem Cells from Skeletal Muscle for the Treatment of Neuromuscular Disease

The major goals of this project are to undertake a cellular and molecular characterization of Pax7+/Myf5-satellite cells, confirm they represent a true stem cell reservoir and investigate their potential for therapeutic exploitation.

Role: PI

CIHR Rudnicki (PI) 10/01/2006 – 09/30/2011

Genomic Investigation of Transcriptional Regulation in Embryonic Stem Cells

The major goals of this grant are to investigate the Oct4 transcriptional network in mESC and to define the post translational mechanisms regulating Oct4 function.

Role: PI

HMI Rudnicki (PI) 01/01/2007 – 12/31/2011

Defining the Molecular Determinants of Myogenic Commitment

The major goals of this project are to define the role played by Histone Methylases as co-regulators of Pax7.

Role: PI

CIHR Rudnicki (PI) 10/01/2007 – 09/30/2012

Genetic Regulation of Myogenesis

The major goals of this project are to define the regulons of Myf5 and MyoD by identifying target genes, defining their interacting proteins and investigating their function in growth and differentiation.

Role: PI

MDA Rudnicki (PI) 07/01/2008 – 06/30/2011

Molecular regulation of satellite cell function

The major goals of this project are to investigate the function of satellite stem cells in mdx mouse models of muscular dystrophy and examine the role of Wnt signalling to ameliorate muscle disease.

Role: PI

### **Completed Research Support**

CIHR Rudnicki (PI) 01/10/2004 – 30/09/2009

Genomic Analysis of Rb-family Function in Myogenesis

The major goals of this grant are to further investigate the role played by the Rb-family by isolating and characterizing muscle progenitors which specifically lack these genes and to identify target genes whose expression is directly regulated by Rb-family genes.

Role: PI

R01 AR 44031-09A1 Rudnicki (PI) 04/01/2005 – 03/30/2010

NIH/NIAMS

Genetic Regulation of Skeletal Muscle Repair

The major goals of this project are to undertake a molecular analysis of Pax7 function and to identify Pax7 target genes.

Role: PI