

Principal Investigator/Program Director (Last,
FIRST NAME)

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.

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NAME	POSITION TITLE		
Muthu Periasamy, Ph.D.	Professor and Chair, Department of Physiology and Cell Biology College of Medicine and Public Health , Ohio State University , Columbus, OH		
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Faculty de Sciences Univ. of Montpellier, Montpellier. France	Ph.D.	1978	Biochemistry
Albert Einstein College of Medicine, New York, NY and Harvard Medical School, Boston, MA	Postdoc	1980-84	Molecular Genetics and Molecular Cardiology

POSITIONS AND HONORS

Positions and Employment

1984-1985 Instructor, Dept. of Cardiology, Harvard Medical School, Boston, MA.
1986-1992 Assistant Professor, Department of Physiology & Biophysics, University of Vermont, Burlington, VT.
1992-1992 Associate Professor, Department of Physiology & Biophysics, University of Vermont.
1992-1996 Associate Professor, Department of Internal Medicine and Molecular Genetics, Biochemistry &
Microbiology, University of Cincinnati.
1992-2001 Director of Molecular Cardiology, Division of Cardiology, University of Cincinnati.
1996-2001 Professor of Medicine, Department of Internal Medicine and Pharmacology /Cell Biophysics University of
Cincinnati.
2001-Present Professor and Chair, Department of Physiology and Cell Biology, Ohio State University, Columbus
Associate Director, Davis Heart & Lung Research Institute, College of Medicine & Public Health, Ohio
State University, Columbus

Other Experience and Professional Membership

French Cultural and Scientific Exchange Fellowship (Ph.D. student), France, 1975-1978
AHA Established Investigator Award, 1988-1992
Member. NHLBI- Program Project Review Committee . (1992 -1996)
Visiting Professor - University of Paris-Sud, France, 1997
NIH Study Section CVA, CVB,(ad hoc, 1989-1991), NIH Committee on Centers for Vascular Biology and Medicine, 1992
ISHR Council Member – 1998 - 2003
NIH Study Section –CVB 2000-2004
NIH Study Section – CCHF 2004-present

Editorial Consultant

Principal Investigator/Program Director (Last, First, Middle):

Circulation Research (Editorial Board), Journal of Molecular and Cellular Cardiology (Associate Editor), Japanese Heart Journal (Editorial Board) Guest Reviewer: Journal of Molecular Biology, Nature-Medicine, Nucleic Acids Research, Journal of Cell Biology, Journal of Biological Chemistry, Proceedings of National Academy of Sciences.

PUBLICATIONS: (Selected publications from a total of 100 since 1982)

Nagai R, Larson DM, Periasamy M. Characterization of a mammalian smooth muscle myosin heavy chain cDNA clone and its expression in various smooth muscle types. Proc. Natl. Acad. Sci., USA 85:1047-1051, 1988.

Nagai R, Herzberg AZ, Brandl CJ, Fuji J, Tada M, MacLennan DH, Alpert NR, Periasamy M. Regulated expression of myocardial SR Ca²⁺ ATPase and phospholamban in response to pressure overload and thyroid hormone. Proc. Natl. Acad. Sci., USA 86:2966-2970, 1989.

Lytton J, Herzberg AZ, Periasamy M, MacLennan DH. Molecular cloning of sarco(endo)plasmic reticulum Ca²⁺ ATPase from rabbit uterine smooth muscle. J. Biol. Chem. 264:7059-7065, 1989.

- Zarain-Herzberg A, MacLennan DH, Periasamy M. Characterization of rabbit cardiac sarco(endo)plasmic reticulum Ca^{2+} ATPase gene. J. Biol. Chem. 17:7723-7734, 1990.
- Arai M, Otsu K, MacLennan DH, Alpert NR, Periasamy M. Effect of thyroid hormone on the expression of mRNA encoding sarcoplasmic reticulum proteins. Circ. Res. 69:266-276, 1991.
- Arai M, Alpert NR, and Periasamy M. Cloning and characterization of the gene encoding rabbit cardiac calsequestrin. Gene. 109:275-279, 1991.
- Arai M, Otsu K, MacLennan DH, and Periasamy M. Regulation of sarcoplasmic reticulum gene expression during cardiac and skeletal muscle development. Am. J. Physiol. C614-C620, 1992.
- Nagai, R., Babij, P., and Periasamy, M. Identification of two types of smooth muscle myosin heavy chain isoforms by cDNA cloning and immunoblot analysis. J. Biol. Chem. 264:9734-9737, 1989.
- Sukovich D, Shabbeer J, and Periasamy M. Analysis of the rabbit cardiac/slow twitch muscle sarcoplasmic reticulum calcium ATPase (SERCA2) gene promoter. Nucleic Acids Res. 21:2723-2728, 1993
- Arai M, Matsui H, Periasamy M. Sarcoplasmic reticulum gene expression in cardiac hypertrophy and heart failure. Circ. Res. 74:555-564, 1994.
- Zarain-Herzberg A, Marques J, Sukovich D, Periasamy M. Thyroid hormone receptor modulates the expression of the rabbit cardiac sarco(endo)plasmic reticulum Ca^{2+} ATPase gene. J. Biol. Chem. 269:11674, 1994.
- Matsui, J., MacLennan, D.H., Alpert, M.R., Periasamy, M. Sarcoplasmic reticulum gene expression in pressure overload cardiac hypertrophy in rabbits. Am. J. Physiol. C-252-258, 1995.
- Khoury, S.F., Hoit, B.D., Dave, V., Shao, Y., Gabel, M., Periasamy, M., Walsh, R.A. The effects of thyroid hormone on left ventricular performance and steady state mRNA levels for the contractile and calcium cycling proteins in the baboon. Circ. Res. 79:727-735, 1996.
- Baker, D.L., Dave, V., Reed, T., Periasamy, M. Multiple SP1 binding sites in the cardiac/slow twitch muscle SR Ca^{2+} -ATPase (SERCA2) gene promoter are required for expression in SOL8 muscle cells. J. Biol. Chem. 271:5921-5928, 1996.
- Baker D, Dave V, Reed T, Misra S, and Periasamy M. A novel E-box/AT-rich element is required for the muscle specific expression of the sarcoplasmic reticulum Ca^{2+} ATPase (SERCA2) gene. Nucl. Acids Res. 26:1092-1098, 1998.
- Baker DL, Grupp IL, Ji Y, Reed T, Loukianov E, Grupp G, Bhagwat A, Hoit B, Walsh R, and Periasamy, M. Targeted overexpression of the sarcoplasmic reticulum Ca^{2+} ATPase increases cardiac performance in transgenic mouse hearts. Circ. Res. 83:1205-1214, 1998.
- Loukianov E, Ji Y, Grupp IL, Baker DL, Loukianova T, Grupp G, Lytton J, and Periasamy M. Enhanced myocardial performance and increased Ca^{2+} transport function in transgenic hearts expression the fast-twitch skeletal muscle sarcoplasmic reticulum Ca^{2+} ATPase. Circ. Res. 83:889-897, 1998.
- Rishi AK, Wu JT, Yu M, Belani JP, Fontana JA, Baker D, Periasamy M, and Hussain A. Gene amplification and transcriptional upregulation of the sarco/endoplasmic reticulum Ca^{2+} transport ATPase in thapsigargin-resistant hamster smooth muscle cells. Nucl. Acids Res., 26:4529-4537, 1998.
- Loukianov E, Ji Y, Baker DL, Reed T, Babu J, Loukianova T, Greene A, Shull G and Periasamy M. Sarco (endo) plasmic reticulum Ca^{2+} ATPase isoforms and their role in muscle physiology and pathology. Ann n y Acad. Sci. 16;853:251-9, 1998.
- Periasamy M, Reed TD, Liu LH, Ji Y, Loukianov E, Paul RJ, Nieman ML, Miller ML, Riddle T, Duffy JJ, Doetschman T, Norenz JN, and Shull GE. Impaired cardiac performance in heterozygous mice with a null mutation in sarco(endo) plasmic reticulum Ca^{2+} -ATPase isoform 2 (SERCA2) gene. J. Biol. Chem. 274:2556-2562, 1999.
- Ji Yong, Loukianov E, Loukianova T, Jones LR, and Periasamy M. SERCA1a can functionally substitute for SERCA2a in the heart. Amer. J. Phys. 276:H89-H97, 1999

- Ji Y, Loukianov E, and Periasamy M. Analysis of sarcoplasmic reticulum Ca^{2+} transport and Ca^{2+} ATPase enzymatic properties using mouse cardiac tissue homogenates. *Anal. Biochem.* 269, 236-244, 1999.
- Takeishi Y, Bhagwat A, Ball NA, Kirkpatrick DL, Periasamy M, and Walsh RA. Angiotensin converting enzyme inhibition attenuates translocation of PKC aneins in pressure-overload heart failure. *Am. J. Phys.* 276:H53-62, 1999.
- Aoyagi T, Yonekura K, et al. The sarcoplasmic reticulum Ca^{2+} -ATPase (SERCA2) gene promoter activity is decreased in response to severe left ventricular pressure-overload hypertrophy in rat hearts. *J. Mol. Cell. Cardiol.* 31:919-926, 1999.
- Ji Y, Lalli MJ, Babu GJ, Xu Y, Kirkpatrick DL, Liu LH, Chiamvimonvat N, Walsh RA, Shull GE, and Periasamy M. Disruption of a single copy of the SERCA2 gene results in altered Ca^{2+} homeostasis and cardiomyocyte function. *J. Biol. Chem.* 275:38073-38080, 2000.
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- Reed TD, Babu GJ, Ji Y, Zilberman A, Ver Heyen M, Wuytack F and Periasamy M. The expression of SR calcium transport ATPase and the $\text{Na}^{+}/\text{Ca}^{2+}$ Exchange are antithetically regulated during mouse cardiac development and in Hypo/hyperthyroidism. *J. Mol. Cell Cardiol.* 32(3):453-64, 2000.
- Geene AL, Lalli MJ, Ji Y, Babu GJ, Grupp I, Sussman M and Periasamy M. Overexpression of SERCA2b in the heart leads to an increase in sarcoplasmic reticulum calcium transport function and increased cardiac contractility. *J. Biol. Chem.* 11;275(32):24722-7, 2000.
- Hashimoto K, Perez NG, Kusuoka H, Baker DL, Periasamy M and Marban E. Frequency-dependent changes in calcium cycling and contractile activation in SERCA2a transgenic mice. *Basic Res. Cardiol.* 95(2):144-51, 2000.
- Liu LH, Boivin GP, Periasamy M and Shull GE. Squamous cell tumors in mice with a single null allele of *Atp2a2*, encoding the SERCA2 Ca^{2+} pump. *J. Biol. Chem.* 276(29): 26737-40, 2001.
- Babu, GJ, Loukianov E, Loukianova T, Pyne GJ, Huke S, Osol G, Low RB, Paul RJ and Periasamy M. Loss of SM-B myosin isoform results in a decrease of maximal force development and velocity of shortening. *Nature Cell Biol.* Vol 3:1025-1029, 2001.
- Periasamy M. Adenoviral-mediated serca gene transfer into cardiac myocytes: how much is too much? *Circ. Res.* 2;88 (4):373-5, 2001.
- M. Jane Lalli, Ji Yong, Katsuji Hashimoto, Gopal J. Babu, Darryl Kirkpatrick, Evgenij Loukianov, Richard A. Walsh, Mark Sussman, Eduardo Marban, Muthu Periasamy. SERCA1a Structurally Substitutes for SERCA2a in the Cardiac Sarcoplasmic Reticulum and Increases Cardiac Ca^{2+} Handling Capacity. *Circulation Research* 89(2):160-7, 2001.
- Periasamy M and Huke S. SERCA pump is a critical determinant of Ca^{2+} homeostasis and cardiac contractility. *J. Mol. Cell Cardiol.* 33:1053-1063, 2001.
- Huke S, Prasad V, Nieman ML, Nattamai KJ, Grupp IL, Lorenz JN and Periasamy M. Altered dose response to beta-agonists in SERCA1a-expressing hearts ex vivo and in vivo. *Am J physiol Heart Circ Physiol* 283(3):H958-65, 2002.
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- Zhao W, Frank KF, Chu G, Gerst MJ, Schmidt AG, Ji Y, Periasamy M and Kranias EG. Combined Phospholamban Ablation and SERCA1a Overexpression Result in a New Hyperdynamic Cardiac State. *Cardiovasc Res.* 57(1): 71-81, 2003.

Principal Investigator/Program Director (Last, First, Middle):

Takizawa T, Arai M, Tomaru K, Koitabashi N, Baker DL, Periasamy M and Kurabayashi M. Transcription Factor Sp1 Regulates SERCA2 Gene Expression in Pressure-Overload Hearts: A Study using *In Vivo* Direct Gene Transfer Into Living Myocardium. *J Mol Cell Cardiol.* :35(7) 777-783, 2003.

Zhou Y, Dirksen WP, Babu GJ and Periasamy M. Differential vasoconstrictions induced by angiotensin II: the role of AT1 and AT2 receptors in isolated C57BL/6J mouse blood vessels. *Am J Physiol Heart Circ Physiol* 285(6):H2797-H2803, 2003.

Zhou Y, Chen Y, Dirksen WP, Morris M and Periasamy M. AT1b Receptor Predominantly Mediates Contractions in Major Mouse Blood Vessels. *Circ Res* 93(11):1089-94, 2003.

Schultz JE, Glascock BJ, Witt SA, Nieman ML, Nattamai KJ, Liu LH, Lorenz JN, Shull GE, Kimball TR and Periasamy M. Accelerated onset of heart failure in mice during pressure overload with chronically decreased SERCA2 calcium pump activity. *Am J Physiol Heart Circ Physiol* 286: H1146-H1153, 2004.

Research Support

Ongoing Research Support

R01 HL-64140-06 Periasamy (PI) 01/01/2004-12/31/2007
NIH/NHLBI

SR Ca²⁺ ATPase, a critical determinant of cardiac contractility

The major goals of this proposal are 1) to generate a conditional KO for SERCA2 gene and determine how loss of SERCA pump affect cardiac function in adult heart, 2) to define the role of SERCA2a and SERCA2b isoforms in cardiac contractility and, 3) to determine the SERCA protein complex using proteomics and mass spectrometry.

Role: PI

R01 5 R01-HL38355-16 Periasamy (PI) 01/01/01-12/31/05
NIH/NHLBI

Molecular analysis of smooth muscle myosin

The major goal of this proposal is to understand structure/function relationship of smooth muscle myosin isoforms. We have chosen a transgenic approach to develop models deficient in N-terminal and or carboxy-terminal isoforms.

Role: PI