

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.

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NAME R. John Solaro		POSITION TITLE	
eRA COMMONS USER NAME SOLARORJ		University Professor and Head	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Univ. of Cincinnati, Cincinnati, OH	B.Sc.	1965	Pharmacy
Univ. of Pittsburgh, School of Medicine	Ph.D.	1971	Physiology
Univ. of Birmingham, Birmingham, England	----	1975-76	Biochemistry

ACADEMIC APPOINTMENTS

Instructor (1972-73); Assistant Professor (1973-77), Department of Physiology, Medical College of Virginia. **British-American Heart Fellow (1975-76)**, Department of Biochemistry, University of Birmingham, England. **Associate Professor (1977); Professor (1981)**, Department of Physiology and Biophysics, University of Cincinnati, College of Medicine. **Senior International Fellow of the Fogarty Foundation (1987)**, Department of Physiology, University College, London. **Professor and Head (1988-present)**, Department of Physiology and Biophysics, Co-Director, Center for Cardiovascular Research, University of Illinois, College of Medicine at Chicago. **Co-Director of the UIC Center for Cardiovascular Research (2003-present); Distinguished University Professor (1998-present)**, Department of Physiology and Biophysics, University of Illinois at Chicago, College of Medicine.

HONORS AND ADVISORY COMMITTEES

NIH MERIT Award R37 HL 22231 (12/01/96 – 11/30/06)
 The 1994 Distinguished Faculty Award - UIC College of Medicine
 2008 University of Illinois Mentor of the Year Award
 Intern Acad Cardiovasc Sciences Nagano Award for Excellence in Cardiovasc Ed (2006)
 Associate Editor, *Am J Physiol:Heart* (2005-) (1990-98)
 Associate Editor *J Mol Cell Card* (2008-)
 Editorial Boards, *J. Biol Chem* (2004-) *Circ Research* (1982-88; 1994-); *J Mol Cell Card* (1993-2008); *J Clin Invest* (1998-2002); *Molecular and Cellular Biochemistry* (1992-)
 Board of Directors, Proteomics and Informatics Section: Chicago Biomedical Consortium
 Research Career Development Award of the NIH, 1977-82; AHA Established Invest Award
 Full Member Skeletal Muscle Exercise Physiol Study Section (2007-)
 Full Member and Chair, NIH, Experimental Cardiology Study Section (1988-92)
 Full Member, NIH, Physiology Study Section (1983-7); NIH, Clin Sciences Study Section (1980-2)
 Biophysical Society (Chair, Public Affairs Committee 2008-2010)
 Biophysical Society, Council (2005-2008); Co-Chairman, Contractility Subgroup (1983-84)
 ISHR American Section: (Council 2006-2012; Secretary 1994; Council 1985-94;) Cardiac Muscle Society (Secretary/Treasurer, 1983-84; President, 1985-86)
 International Society for Heart Research (ISHR) Secretary General 1995-8;
 Association of Chairs of Departments of Physiology (Sec/Treas 1994-97; President 1999).

Selected Publications Last 3 years out of 289 papers.

- Solaro RJ, Arteaga GM. (2007) Heart failure, ischemia/reperfusion injury and cardiac troponin. *In: Regulatory mechanisms of Striated Muscle Contraction* (Ebashi S, Ohtsuki I, eds.) Adv Exp Med Biology 592:191-200. Springer (Tokyo) PMID: 17278366
- Bupha-Intr T, Wattanapermpool J, Pena JR, Wolska BM, Solaro RJ. (2007) Myofilament response to Ca²⁺ and Na⁺/H⁺ exchanger activity in sex hormone elated protection of cardiac myocytes from deactivation in hypercapnic acidosis. *Am J Physiol (Reg Integ)*. 292 :R837-43. PMID: 17038443
- Engel PL, Kobayashi T, Biesiadecki B, Davis J, Tikunova S, Wu S, Solaro RJ. (2007) Identification of a region of troponin I important in signaling cross-bridge dependent activation of cardiac myofilaments. *J Biol Chem*. 282:183-93. PMID: 17099250
- Vahebi S, Ota A, Li M, Warren CM, de Tombe PP, Want Y, Solaro RJ. (2007) p38-MAPK Induced Dephosphorylation of Alpha-Tropomyosin is Associated with Depression of Myocardial Sarcomeric Tension and ATPase Activity. *Circ Res* 100:408-15. PMID: 17234967
- Hinken A, Solaro RJ. (2007) A Dominant Role of Intrinsic Regulation of Cardiac Molecular Motors in the Control of Ventricular Ejection and Relaxation. *Physiology* 22:73-80. PMID: 17420299
- Davis JP, Alionte C, Kobayashi T, Solaro RJ, Swartz DR, Tikunova SB. (2007) Effects of thin and thick filament proteins on calcium binding and exchange with cardiac troponin C. *Biophysical J* 92:3195-206. PMID: 17293397
- Ke Y, Lum H, Solaro, RJ. (2007) Dephosphorylation of Myosin regulatory Light Chain and Inhibition of Barrier Dysfunction Induced by P²¹ Activated Kinase-1 in Endothelial Cells. *Canadian J Physiol and Pharm*. 2007 ;85:28128. PMID: 17612635
- Ke Y, Lei M, Collins TP, Rakovic S, Mattick PAD, Yamasaki M, Brodie MS, Terrar DA, Solaro RJ. (2007) Regulation of L-type calcium channel and delayed rectifier potassium channel activity by P²¹ activated kinase-1 in guinea-pig sino-atrial node pacemaker cells. *Circ Res*. 100:1317-27 PMID: 17413045
- Jagatheesan G, Rajan S, Petrashevskaya N, Schwartz A, Boivin G, Arteaga GM, Solaro RJ, Liggett SB, Wieczorek DF. (2007) Rescue of tropomyosin-induced familial hypertrophic cardiomyopathy mice by transgenesis. *Am J Physiol Heart Circ Physiol*. 293: H949-H958. PMID: 17416600
- Biesiadecki BJ, Kobayashi T, Walker JS, Solaro RJ, de Tombe PP. Troponin C G159D Mutation Blunts Myofilament Desensitization induced by Troponin I PKA Phosphorylation. *Circ Res* 2007; 100:1486-93. PMID: 17446435
- Xiao L, Zhao Q, Du Y, Chao Y, Solaro RJ, Buttrick PM. (2007) PKC ϵ increases phosphorylation of the cardiac myosin binding protein C at Serine 302 both *in vitro* and *in vivo*. *Biochemistry* 2007; 46:7054-7061. May 16; [Epub ahead of print] PMID: 17503784
- Rajan S, Ahmed RPH, Jagatheesan G, Petrashevskaya N, Boivin GP, Urboniene D, Arteaga GM, Wolska BM, Solaro RJ, Liggett SB, Wieczorek DF. Dilated cardiomyopathy mutant tropomyosin mice develop cardiac dysfunction with significantly decreased fractional shortening and myofilaments calcium sensitivity. *Circ Res* 2007;101:205-214. June 7 [Epub ahead of print] PMID: 17556658
- Belin RJ, Sumandea MP, Allen EA, Schoenfelt K, Wang H, Solaro RJ, de Tombe PP. Augmented protein kinase C-alpha induced myofilament protein phosphorylation contributes to myofilaments dysfunction in experimental congestive heart failure. *Circ Res* 2007; 101:195-204. PMID: 17556659
- Sheehan KA, Ke Y, Solaro RJ. P²¹ Activated kinase-1 and its role in integrated regulation of cardiac contractility. *Am J Physiol. Am J Physiol Regul Integr Comp Physiol*. 2007 293:R963-73. PMID: 17609315
- Howarth JW, Meller J, Solaro RJ, Trehwella J, Rosevear PR. Phosphorylation -dependent conformational transition of the cardiac specific n-extension of troponin I in cardiac troponin. *J Mol Biol*. 2007; 373: 706-722. PMID: 17854829
- Wu SC, Solaro RJ. (2007)Protein Kinase C Zeta: A Novel Regulator Controlling Both Phosphorylation and De-Phosphorylation of Cardiac Sarcomeric Proteins. *J Biol Chem* 2007; 282: 306918 PMID: 17724026.
- Warren CM, Arteaga GM, Rajan S, Ahmed RPH, Wieczorek DF, Solaro RJ. (2008) Use of 2D-DIGE analysis reveals altered phosphorylation in tropomyosin mutant (Glu54Lys) linked to dilated cardiomyopathy. *Proteomics*. 8:100-105. PMID: 18095372
- Solaro RJ, Rosevear, Kobayashi T. (2008) The unique functions of cardiac troponin I in the control of

- cardiac muscle contraction and relaxation. *Biochem Biophys Res Commun.* 369: 82-87. PMID: 18162178.
- Solaro RJ, deTombe PP. (2008) Review focus series: sarcomeric proteins as key elements in integrated control of cardiac function. *Cardiovasc Res.* 2008 Mar 1;77(4):616-8. PMID: 18192242
- Nowak G, Pena JR, Urboniene D, Geenen DL, Solaro RJ, Wolska BM. (2008) Correlations Between Alterations in Length-Dependent Ca^{2+} Activation of Cardiac Myofilaments and the End-Systolic Pressure-Volume Relation. *J Mus Res Cell Motility* 28:415-9. PMID: 18365757
- Tachampa K, Kobayashi T, Wang H, Martin A, Biesiadecki B, Solaro RJ, de Tombe PP. (2008) Increased crossbridge cycling kinetics after exchange of C-terminal truncated troponin-I in skinned rat cardiac muscle. *J Biol Chem* 283:15114-15121. PMID: 18378675
- Yuan C, Solaro RJ. (2008) Myofilament proteins: From cardiac disorders to proteomic changes. *Proteomics Clin Appl* 2: 788-799
- Ke Y, Solaro RJ. (2008) Use of a Decoy Peptide to purify p21 activated Kinase-1 in cardiac muscle and Identification of ceramide related activation. *Biological Targets and Therapy* (In Press).
- Yuan C, Sheng Q, Tang H, Li Y, Zeng R, Solaro RJ. Quantitative Comparison of Sarcomeric Phospho-Proteomes of Neonatal and Adult Rat Hearts. *Am J Physiol Heart Circ Physiol.* 2008 Jun 13. [Epub ahead of print] PMID: 18552161
- Sumandea MP, Rybin VO, Hinken AC, Wang C, Kobayashi T, Harleton E, Sievert G, Balke CW, Feinmark SJ, Solaro RJ, Steinberg SF. Tyrosine phosphorylation modifies PKCdelta -dependent phosphorylation of cardiac troponin I. *J Biol Chem.* 283(33):22680-9 Jun 12. [Epub ahead of print] PMID: 18550549
- Solaro RJ. (2008) Multiplex Kinase Signaling Modifies Cardiac Function at the level of Sarcomeric proteins. *J. Biol Chem.* 283:26829-33. Epub 2008 Jun 19. PMID: 18567577
- Sheehan, KA, Ke Y, Wolska BM, Solaro RJ. (2009) Expression of Active p^{21} -Activated Kinase-1 (Pak1) Induces Ca^{2+} -flux Modification with Altered Regulatory Protein Phosphorylation in Cardiac Myocytes. *Am J Physiol (Cell)* 296:C47-C58. Oct 15. [Epub ahead of print] PMID: 18923061.
- Baudenbacher F, Schober T, Pinto JR, Sidorov VY, Hilliard F, Solaro RJ, Potter JD, Knollman BC. (2008) Myofilament calcium sensitization causes susceptibility to cardiac arrhythmia. *J Clin Invest.* 2008; 118 3893-903 Nov 20. [Epub ahead of print] PMID: 19023433
- Ke, Y, Solaro RJ. (2009) Use of a Decoy Peptide to Purify p21 activated Kinase-1 in Cardiac Muscle and Identification of Ceramide Related Activation. *Biologics: Targets and Therapy* 2:903-909.
- Solaro RJ. (2009) Maintaining cooperation among cardiac myofilament proteins through thick and thin. *J. Physiol (London)* 587.1: 3. PMID: 19119179
- Scruggs SB, Hinken AC, Thawornkaiwong A, Robbins J, Walker LA, de Tombe PP, Geenen DL, Buttrick PM, Solaro RJ. (2009) Ablation of ventricular myosin regulatory light chain phosphorylation in mice causes cardiac dysfunction in situ and affects neighboring myofilament protein phosphorylation. *J Biol Chem.* 284:5097-106. 2008 Dec 23. [Epub ahead of print] PMID: 19106098
- Solaro RJ. (2009) CK-1827452, a sarcomere-directed cardiac myosin activator for acute and chronic heart disease. *IDrugs* 12: 243-251. PMID: 19350469
- Engel PL, Hinken A, Solaro RJ. (2009) Differential Effects of Phosphorylation of Regions of Troponin I in Modifying Cooperative Activation of Cardiac Thin Filaments *J Mol Cell Cardiol* Sep;47(3):359-64. Epub 2009 May 5. PMID: 19426736 [PubMed - indexed for MEDLINE] .
- Kirk JA, Macgowan GA, Evans C, Smith SH, Warren CM, Mamidi R, Chandra M, Stewart AF, Solaro RJ, Shroff SG. (2009) Left Ventricular and Myocardial Function in Mice Expressing Constitutively Pseudophosphorylated Cardiac Troponin I *Circ Res.* 105:1232-1239. PMID: 19850940
- Egom EE, Ke Y, Musa H, Mohamed TM, Wang T, Cartwright E, Solaro RJ, Lei M. FTY720 prevents ischemia/reperfusion injury-associated arrhythmias in an ex vivo rat heart model via activation of Pak1/Akt signaling. *J Mol Cell Cardiol.* 2009 Oct 21. [Epub ahead of print] PMID: 19852968
- Lee DI, Vahebi S, Tocchetti CG, Barouch LA, Solaro RJ, Takimoto, E, Kass DA. (2010) β -3-PKG-Troponin I Phosphorylation Underlies PDE5A Modulation of Myocyte β -Adrenergic Stimulation. *Basic Res Cardiol* (In Press)
- Rajan S, Jagatheesan G, Karam CN, Alves ML, Bodi I, Schwartz A, Bulcao CF, D'Souza KM, Akhter SA, Boivin GP, Dube DK, Petrashevskaya N, Herr AB, Hullin R, Liggett SB, Wolska BM, Solaro RJ, Wieczorek DF. Molecular and Functional Characterization of a Novel Cardiac Specific Human Tropomyosin. *Circulation.* 2010 Jan 11. [Epub ahead of print] PMID: 20065163

CURRENT SUPPORT

• Modulation of Calcium Control of Cardiac Myofibrils

Principal Investigator: R. John Solaro, Ph.D.

Agency: NIH Type: RO1 HL 22231 (29-32)

Period: 12/01/06 - 11/30/10 \$180,000 per year

This project is an RO1 renewal of a MERIT Award and tests the hypothesis that myofilament response to Ca^{2+} is a significant regulator of cardiac contraction level and dynamics.

• Integrated Mechanisms of Cardiac Maladaptation

Principal Investigator: R. John Solaro, Ph.D.

Agency: NIH Type: 1 PO1 HL 62426 (06-10)

Period: 06/01/05-05/31/10 \$227,000/year

Project Leader "Ca²⁺-Signaling in Cardiac Myofilaments" and Leader of Administrative Core A
(Renewal priority score 20; cutoff listed as 25)

Our hypothesis is that altered signaling at the level of sarcomere proteins occurs in the course of compensation to hemodynamic stressors leading to hypertrophy and is a significant factor in the decompensation leading to pump failure. The objectives test the idea that altered phosphorylation of cTnI and alterations at the Z-disc are among these significant factors.

• Troponin Modulation in Heart Failure

Principal Investigators: R. John Solaro, Ph.D. and Beata M. Wolska, PhD

Agency: NIH Type: 5 R01 HL64035 (11-14) (Multiple PI)

Period: 1/01/10-12/31/13 \$250,000/year

The project investigates the role of Pak1 in control of cardiac EC coupling and mechanisms of rescue of DCM and HCM phenotype in mouse models on inherited cardiomyopathies. .

• Regulation of Sarcomeric Function by Tropomyosin

Principal Investigator David Wiczorek, PhD University of Cincinnati

Agency NIH Type: RO1 HL 081680

Period: 07/07-06/11 \$;87,000/year

Subcontract: Principal Investigator: R. John Solaro, PhD 10% Effort

This proposal investigates effects of isoform composition and post-translational modifications of tropomyosin in various transgenic models.

Aim. To determine mechanical changes in sarcomeres expressing pseudo-phosphorylated tropomyosin.

NIH TypeT32 HL 07692-16-20

• Cellular Signaling in the Cardiovascular System

Principal Investigator: R. John Solaro, PhD

Major goals: Training program with 7 pre-doc and 7 post-doc slots to provide investigators with the background training and skills to advance knowledge related to the understanding, prevention, and treatment of cardiovascular disease.

Period: 07/05-06/10

Annual direct costs: \$ 664, 942