BIOGRAPHICAL SKETCH

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NAME Padmini Komalavilas	POSITION TITLE Research Scientist Research Associate Professor
eRA COMMONS USER NAME padkom	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Madras-India	B.S.	1975-1978	Chemistry
University of Madras-India	M.S.	1978-1980	Biochemistry
Oklahoma State University, Stillwater, OK	Ph.D	1984-1988	Biochemistry
University of California, Riverside, CA	Postdoctoral	1988-1990	Biochemistry
University of South Alabama, Mobile, AL	Postdoctoral	1990-1992	Physiology

A. Personal Statement:

Dr. Komalavilas is a biochemist and a smooth muscle physiologist, with over 20 years of research experience in studying smooth muscle physiology and biochemistry. Dr. Komalavilas's research focuses on the signaling pathways of smooth muscle relaxation to develop therapeutics for diseases such as asthma and vasospasm. Her research efforts have identified several novel aspects of the cross talk of signaling events in smooth muscle contractility. She has 47 publications in peer reviewed journals in smooth muscle research. Dr. Komalavilas and colleagues were the first to demonstrate that small heat shock protein 20 is a substrate for cAMP kinase in airway smooth muscle and that forskolin induced phosphorylation of heat shock protein 20 mediates relaxation of bovine airway smooth muscle. She has recently demonstrated that a phospho-peptide analog of HSP20 relax human airway smooth muscle even when the beta 2 adrenergic pathway is inhibited suggesting that this peptide has great potential to be a therapeutic for patients for whom the currently used beta agonists are not effective mainly due to desensitization of the receptor. This peptide also decreases airway hyper responsiveness (AHR) in a murine model of asthma. This project will continue her efforts in developing this peptide as a therapeutic for management of airway constriction in asthma. The expertise and experience accumulated in muscle physiology and biochemistry over the years will help in completing the aims of this proposal "Small heat Shock Proteins in Human Airway Smooth Muscle Tone and Pathophysiology". She also has established collaborations with other scientists in Biomedical engineering, Allergy Pulmonary, and Critical Care Medicine, Biochemistry and Molecular Biology to advance her research and have demonstrated ability for independent research in this field of study. Dr. Komalavilas has completed grant from AHA and has been a co-investigator on Federal grants in smooth muscle physiology. She has trained Post Doctoral Fellows, Residents, Graduate students, and undergraduate students. She was also involved in programs that train minority undergraduate students and high school students in research.

B. Positions and Honors.

1992-1996 Research Associate, Department of Pathology, University of Alabama at Birmingham, AL.
1996-2000 Research Instructor, Department of Pathology, University of Alabama at Birmingham, AL.
2000-2001 Research Scientist, Institute of Molecular Medicine and Genetics, Medical College of Georgia, Augusta, GA.
2001-2006 Adjunct Professor, Harrington Dept. of Bioengineering, Arizona State University, Tempe, AZ.
2001-2008 Research Health Scientist, Carl T. Hayden VA Medical Center, Phoenix, AZ.
2006-2008 Research Associate Professor, Harrington Dept. of Bioengineering, Arizona State University, Tempe, AZ.
2007-2008: Consultant, Orthologic, LLC., Tempe, AZ

2008-2012: Research Associate Professor (Adjunct), Arizona State University, Center for Metabolic Biology, Tempe, AZ 85287
2008-current: Research Associate Professor, Vanderbilt University Medical Center, Department of Surgery, Nashville, TN 37232
2008-current: Research Health Scientist, Department of Veterans Affairs Medical Center, Nashville, TN 37212

1978 Merit Scholar
1987 Phi Lambda Upsilon Honorary Chemical Society.
1988 National Dean's List
1988 Member of the Honor Society of Phi Kappa Phi.
1993 American Heart Association, Alabama Affiliate, Fellowship, 1993-95.
1993 The Harriet P. Dustan Fellowship Award. 1993.
1995 Sterling's Who's Who
1997 American Heart Association, Grant in aid.

Other Activities/Committees: Sigma Xi, Treasurer, 1996-98.
VA Safety Review Subcommittee, 2006 -2008
Ad Hoc Reviewer: American Journal of Respiratory Cell and Molecular Biology, Respiratory Research, Pharmacology and Therapeutics, Journal of Biomedicine and Biotechnology, Journal of Surgical Research, Neuroscience Letters

C. Peer-reviewed publications (selected from a total of 44).

1. Komalavilas P, Lincoln TM. Phosphorylation of the inositol 1,4,5-trisphosphate receptor by cyclic GMP-dependent protein kinase. *J Biol Chem*. 1994;269(12):8701-7.
2. Komalavilas P, and Lincoln TM. 1996. Phosphorylation of the inositol 1,4,5 trisphosphate receptor: Cyclic GMP-dependent protein kinase mediates cAMP and cGMP dependent phosphorylation in the intact rat aorta. *J. Biol. Chem*. 271: 21933-21938.
3. Komalavilas P, Mehta S, Wingard CJ, Dransfield D.T, Bhalla J, Woodrum JE, Molinaro JR, Brophy CM. 2001. PI3 Kinase/Akt modulates vascular smooth muscle tone via cAMP signaling pathways, *J Appl Physiol* 91: 1819-1827, 2001.
4. Brophy CM, Woodrum D, Pollock JS, Dickinson M, Komalavilas P, Cornwell TL, Lincoln TM. 2002. Restoration of contractile function to cultured smooth muscle cells by cyclic GMP-dependent protein kinase expression, *J Vasc Res* 39: 95-103.
5. Woodrum DA, Pipkin W, Tessier D, Komalavilas P, Brophy CM. 2003.Phosphorylation of the heat shock-related protein, HSP20, mediates cyclic nucleotide-dependent relaxation. *J Vasc Surg*, 37: 874-81, 2003.
6. Flynn CR, Komalavilas P, Tessier D, Thresher J, Niederkofler EE, Dreiza CM, Nelson RW, Panitch A, Joshi L, Brophy CM. 2003. Transduction of biologically active motifs of the small heat shock-related protein, HSP20, leads to relaxation of vascular smooth muscle. *Faseb J exp,* May 8.
7. Dreiza CM, Brophy CM, Komalavilas P, Furnish EJ, Joshi L, Pallero MA, Murphy-Ullrich JE, von Rechenberg M, Ho YS, Richardson B, Xu N, Zhen Y, Peltier JM, Panitch A. "Transducible heat shock protein 20 (HSP20) phosphopeptide alters cytoskeletal dynamics." *FASEB J*. 19(2):261-3, 2005.
8. Hocking KM, Brophy C, Rizvi RZ, Komalavilas P, Eagle S, Leacche M, Balaguer JM, and Cheung-Flynn J, 2010. Detrimental effects of mechanical stretch on smooth muscle function in saphenous vein. *J. Vas Surg*; 53, 454-60, 20. PMCID 3053010
9. Muto A, Panitch A, Kim N, Park K, Komalavilas P, Brophy CM, and Dardik A. 2012. Inhibition of Mitogen Activated Protein Kinase Activated Protein Kinase II with MMI-0100 reduces intimal hyperplasia ex vivo and in vivo, *Vascular Pharmacology*, 56, 47-55. PMCID: 3268886
10. Osgood MJ, Hocking KM, Voskresensky IV, Li FD, Komalavilas P, Cheung-Flynn J, and Brophy CM, 2013. Surgical vein graft preparation promotes cellular dysfunction, oxidative stress, and intimal hyperplasia in human saphenous vein. *J Vasc Surg*, Jul 30, 2013. PMCID: 3926896.

11. Li FD, Eagle S, Brophy C, Hocking KM, Osgood MJ, Komalavilas P, and Cheung-Flynn J. 2014. *Pressure Control During Preparation of Saphenous Veins.* JAMA Surg, April 25, 2014. PMCID: awaited

Last Author and Publications specific to airway smooth muscle

12. Komalavilas P, Penn R, Flynn CR, Thresher J, Lopes LB, Furnish E, Guo M, Pallero MA, Murphy-Ullrich JE and Brophy CM. 2008. The small heat chock-related protein, HSP20, is a cAMP-dependent protein kinase substrate that is involved in airway smooth muscle relaxation, *Am J Physiol Lung Cell Mol Physiol*, 294: L 69-78. PMCID: 2757925

13. Lopes LB, Brophy, CM, Flynn CR, Yi Z, Bowen BP, Smoke C, Seal BL, Panitch A, Carey C, and, Komalavilas P, 2010. A Novel Cell Permeant Peptide Inhibitor of MAPKAP Kinase II Inhibits Intimal Hyperplasia in a Human Saphenous Vein Organ Culture Model*. J Vas Surg,* 52, 1596-607. PMCID 3005888
14. Li FD, Sexton KW, Hocking KM, Osgood MJ, Eagle S, Cheung-Flynn J, Brophy CM, and Komalavilas P. 2012. *Intimal Thickness Associated with Endothelial Dysfunction in Human Vein Grafts*. *J Srug Res.* PMCID: 3515722.
15. Hocking KM, Putumbaka G, Venkatraman SL, Brophy CM, Cheung-Flynn J, and Komalavilas P, 2013. Role of Cyclic Nucleotide-Dependent Thin Filament Dynamics: Calcium Flux and Force Inhibition in Forskolin-Pretreated Porcine Coronary Arteries*. PLOS ONE*, 2013; 8(4):e60986. PMCID: 3625185.

Issued Patents:

Brophy, *et al*. Reagents and Methods for Smooth Muscle Therapies, USPTO # 7135453 issued November 14, 2006 and USPTO #7381699, issued June 3, 2008. VBLT.P0164US- Improved methods and compositions for vein harvest and autografting.

D. Research Support.

ACTIVE:

R01 HL 105731-01A1(Cheung-Flynn PI) Role: Consultant 02/01/2012-1/31/2016
NIH/HLB1 Methods to reduce vein harvest injury
The aims of this project: 1) Determine the mechanism(s) by which $P2X_7R$ antagonism restores viability and functional responses after stretch injury in porcine saphenous veins (PSV). 2) Determine if stretch injury accelerates intimal hyperplasia and whether $P2X_7R$ blockade will reduce intimal hyperplasia in a porcine vein graft model.

Merit Review Award (PI Brophy) Role: Co I 04/01/13-03/31/17
VA Medical Center "Preservation of Endothelial Dependent Relaxation"
The aims of the project are to: 1) Optimize techniques to preserve HSV endothelial function during surgical preparation and preservation. 2) Determine if optimizing endothelial function during preparation reduces the development of intimal hyperplasia

COMPLETED:

2R01 HL070715 (Brophy PI) Role; Consultant 04/01/08–12/31/14
NIH/NHLBI "Prevention of Vein Graft Spasm"
The aims of this project are to: 1) determine the effect of transducible peptides which inhibit the phosphorylation of HSP27 on smooth muscle physiology, morphology, and biochemistry, 2) determine the effect of optimized peptide mimetics on intimal hyperplasia, 3) determine the molecular mechanisms by which phosphorylated HSP27 "stabilizes" the actin cytoskeleton.

R01 HL070715 (Co I) 04/01/03–03/31/07
NIH/NHLBI "Prevention of Vein Graft Spasm"

The aims of this project (PI. Brophy) are to: 1) Generate recombinant HSP20 linked to a protein transduction domain (PTD) and determine if this engineered protein reverses human vascular smooth muscle spasm ex vivo. 2) Determine the effect of PTD-HSP20 on dynamic cytoskeletal processes relevant to intimal hyperplasia. 3) Determine the feasibility of protein transduction of HSP20 analogues of vein grafts in vivo.

R01 HL58027 (Co PI) 04/01/01-03/31/06
NIH/NHLBI "Heat Shock Proteins and Vasospasm"

The specific aims of this investigation (P.I. Colleen M. Brophy) are to: 1. Characterize the interactions of HSP20 with the smooth muscle contractile apparatus and determine the role of these interactions in mediating vasorelaxation. 2. Determine the mechanisms by which phosphorylated HSP27 inhibits the phosphorylation of HSP20 and muscle relaxation.

AHA ALG970010 (PI). 7/01/97- 06/30/99
American Heart Association, Alabama Affiliate, Inc.
"Regulation of vascular smooth muscle relaxation by cyclic GMP-dependent protein kinase (PKG)"
The goals of the study were (1) to characterize the PKG -dependent phosphorylation of GAP in vitro. (2) To study the in vivo phosphorylation of GAP in intact vascular smooth muscle cells. (3) To define the effects of phosphorylation on the p21 Ras GTPase stimulating activity of GAP.