

2011-2012
Summary of Scholarly Activities
Department of Biochemistry and Molecular Biology

I. PUBLISHED JOURNAL ARTICLES, BOOK CHAPTERS, AND PATENTS

Abe K, Toba M, Alzoubi A, Koubsky K, Ito M, Ota H, Gairhe S, Gerthoffer WT, Fagan KA, McMurtry IF, Oka M. Tyrosine kinase inhibitors are potent acute pulmonary vasodilators in rats. *Am J Respir Cell Mol Biol*. 2011 Oct;45(4):804-8.

Amable L, Grankvist N, Largen JW, Ortsater H, Sjöholm A, Honkanen RE. Disruption of serine/threonine protein phosphatase 5 (PP5:PPP5c) in mice reveals a novel role for PP5 in the regulation of ultraviolet light-induced phosphorylation of serine/threonine protein kinase Chk1 (CHEK1). *J Biol Chem*. 2011 Nov 25;286(47):40413-22.

Chettimada S, Rawat DK, Dey N, Kobelja R, Simms Z, Wolin MS, Lincoln TM, Gupte SA. Glc-6-PDH and PKG contribute to hypoxia-Induced decrease in contractile phenotype proteins and pulmonary artery contraction. *Am J Physiol Lung Cell Mol Physiol*. 2012 Jul;303(1):L64-74.

Cioffi DL, Pandey S, Alvarez DF, Cioffi EA. Terminal sialic acids are an important determinant of pulmonary endothelial barrier integrity. *Am J Physiol Lung Cell Mol Physiol*. 2012 May;302(10):L1067-77.

Cioffi DL, Wu S, Chen H, Alexeyev M, St Croix CM, Pitt BR, Uhlig S, Stevens T. Orail determines calcium selectivity of an endogenous TRPC heterotetramer channel. *Circ Res*. 2012 May 25;110(11):1435-44.

Dodd T, Jadhav R, Wiggins L, Stewart J, Smith E, Russell JC, Rocic P. MMPs 2 and 9 are essential for coronary collateral growth and are prominently regulated by p38 MAPK. *J Mol Cell Cardiol*. 2011 Dec;51(6):1015-25.

Gallos G, Yim P, Chang S, Zhang Y, Xu D, Cook JM, Gerthoffer WT, Emala CW Sr. Targeting the restricted α -subunit repertoire of airway smooth muscle GABAA receptors augments airway smooth muscle relaxation. *Am J Physiol Lung Cell Mol Physiol*. 2012 Jan;302(2):L248-56.

Gerthoffer WT, Schaafsma D, Sharma P, Ghavami S, Halayko AJ. Motility, survival and proliferation. *Compr Physiol*. 2012 Jan;2(1):255-81. Available from: <http://www.comprehensivephysiology.com/WileyCDA/CompPhysArticle/refId-c110018.html>

Gosens R, Stelmack GL, Bos ST, Dueck G, Mutawe MM, Schaafsma D, Unruh H, Gerthoffer WT, Zaagsma J, Meurs H, Halayko AJ. Caveolin-1 is required for contractile phenotype expression by airway smooth muscle cells. *J Cell Mol Med*. 2011 Nov;15(11):2430-42.

Grankvist N, Amable L, Honkanen RE, Sjöholm A, Ortsäter H. Serine/threonine protein phosphatase 5 regulates glucose homeostasis in vivo and apoptosis signaling in mouse pancreatic islets and clonal MIN6 cells. *Diabetologia*. 2012 Jul;55(7):2005-15.

Gupte SA, Wolin MS. Relationships between vascular oxygen sensing mechanisms and hypertensive disease processes. *Hypertension*. 2012 Aug;60(2):269-75.

Hecker PA, Galvao TF, O'Shea KM, Brown BH, Henderson R Jr, Riggle H, Gupte SA, Stanley WC. High-sugar intake does not exacerbate metabolic abnormalities or cardiac dysfunction in genetic cardiomyopathy. *Nutrition*. 2012 May;28(5):520-6.

Huang J, Dou D, Dang J, Pardue JH, Qin X, Huan J, Gerthoffer WT, Tan M. Knowledge acquisition, semantic text mining, and security risks in health and biomedical informatics. *World J Biol Chem*. 2012 Feb 26;3(2):27-33.

Joshi SR, Comer B, McLendon JM, Gerthoffer WT. MicroRNA Regulation of smooth muscle phenotype. *Mol Cell Pharmacol* 2012 4(1):1-16. Available from: <http://www.mcpharmacol.com/index.php/Journals/article/viewFile/159/154>

Lim ST, Miller NL, Chen XL, Tancioni I, Walsh CT, Lawson C, Uryu S, Weis SM, Cheresch DA, Schlaepfer DD. Nuclear-localized focal adhesion kinase regulates inflammatory VCAM-1 expression. *J Cell Biol*. 2012 Jun 25;197(7):907-19.

Mitra A, Menezes ME, Pannell LK, Mulekar MS, Honkanen RE, Shevda LA, Samant RS. DNAJB6 chaperones PP2A mediated dephosphorylation of GSK3 β to downregulate β -catenin transcription target, osteopontin. *Oncogene*. 2012 Oct 11;31(41):4472-83.

Narayanan A, LeClaire LL 3rd, Barber DL, Jacobson MP. Phosphorylation of the Arp2 subunit relieves auto-inhibitory interactions for Arp2/3 complex activation. *PLoS Comput Biol*. 2011 Nov;7(11):e1002226. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3220268/pdf/pcbi.1002226.pdf>

Pung YF, Rocic P, Murphy MP, Smith RA, Hafemeister J, Ohanyan V, Guarini G, Yin L, Chilian WM. Resolution of mitochondrial oxidative stress rescues coronary collateral growth in Zucker obese fatty rats. *Arterioscler Thromb Vasc Biol*. 2012 Feb;32(2):325-34.

Rocic B, Znaor A, Rocic P, Weber D, Lovrencic V. Comparison of antihyperglycemic effects of creatine and glibenclamide in type II diabetic patients. *Wien Med Wochenschr*. 2011 Nov;161(21-22):519-23.

Schneider AM, Rawat D, Weinstein LS, Gupte SA, Richards WO. Effects of laparoscopic Roux-en-Y gastric bypass on glucose-6 phosphate dehydrogenase activity in obese type 2 diabetics. *Surg Endosc.* 2012 Mar;26(3):823-30.

Torres RA, Drake DA, Solodushko V, Jadhav R, Smith E, Rocic P, Weber DS. Slingshot isoform-specific regulation of cofilin-mediated vascular smooth muscle cell migration and neointima formation. *Arterioscler Thromb Vasc Biol.* 2011 Nov;31(11):2424-31.

II. PUBLISHED ABSTRACTS

Ata H, Shrestha D, Oka M, Ochi R, Jong CJ, Gebb S, Benjamin J, Schaffer S, Hobart H, Downey J, McMurtry I, Gupte RS. Down-regulation of replication factor C-40 (RFC40) causes chromosomal missegregation in neonatal and hypertrophic adult rat cardiac myocytes. *FASEB J.* 2012;26:1b85.

Chettimada S, Gupte R, Gupte S. Glucose-6-phosphate dehydrogenase regulates pulmonary artery smooth muscle cell phenotype. *FASEB J.* 2012;26:873.9.

Cioffi EA, Crockett ES, Cioffi DL. Loss of cell-surface sialic acids activates calcium entry in pulmonary endothelial cells. *FASEB J.* 2012;26:1130.9.

Comer BS, Kogut P, Camoretti-Mercado B, Solway J, Halayko, A, Gerthoffer WT. MiR-146a reduces cyclooxygenase-2 expression in human airway smooth muscle cells. *Am J Respir Crit Care Med.* 2012 May 1; 185:A4992. Available from: http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A4992

Dodd TY, Wiggins L, Musiyenko A, Smith E, Rocic P. Increased MMP8 and 12 activation correlates with elevated endostatin and angiostatin and impaired coronary collateral growth in the metabolic syndrome. *FASEB J.* 2012;26:1060.11.

Gupte R. Up-regulation of replication factor C-40 (RFC40) in estrogen positive as well as negative breast cancer. *FASEB J.* 2012;26:1b86.

Hutcheson RL, Smith E, Musiyenko A, Rocic P. miR-mediated regulation of coronary collateral growth in the metabolic syndrome. *FASEB J.* 2012;26:1055.4.

Joshi SR, Abe K, Oka M, McMurtry I, Gerthoffer WT. Micro RNA 145 is differentially regulated in the progression of pulmonary arterial hypertension. *Am J Respir Crit Care Med.* 2012 May 1; 185:A4772. Available from: http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A4772

Kadeba PI, Scammell JG, Cioffi DL. Membrane localization of FK506-binding proteins FKBP51 and FKBP52, immunophilins that are part of the endothelial store-operated calcium entry heterocomplex. *FASEB J.* 2012;26:1130.7.

McLendon JM, Joshi SR, Abe K, Oka M, McMurtry I, Gerthoffer WT. Dysregulated microRNA expression in peripheral blood mononuclear cells of experimental pulmonary arterial hypertension. *Am J Respir Crit Care Med*. 2012 May 1;185:A3407. Available from: http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A3407

Morrow R, Fagan KA, Cioffi DL. Anti-endothelial cell antibodies (AECA) in pulmonary arterial hypertension (PAH). *FASEB J*. 2012;26:873.4.

Ochi R, Gupte SA. Does dehydroepiandrosterone directly inhibit L-type Ca channel current in vascular smooth muscle? *Biophys J*. 2012 Jan 31;102(3,S1):129a. Abstract no. 646-Pos Board B432. Available from: <http://download.cell.com/biophysj/pdf/PIIS0006349511020637>

Ochi R, Gupte SA. L-type Ca²⁺ channel current from on-cell patch is augmented by H₂O₂ in rat aortic smooth muscle-derived A7r5 cells. *FASEB J*. 2012;26:695.4.

Vasauskas AA, Wang X, Chen H, Wu S, Cioffi DL. The serine-threonine calcium/calmodulin-activated phosphatase calcineurin is involved in regulation of store-operated calcium entry. *FASEB J*. 2012;26:1130.6.

Vimercati C, Qanud K, Gupte R, Patel N, Khan R, Pfeffer M, Maioli M, Cioffi E, Gupte S, Recchia FA. Short interfering RNA-mediated knockdown of Glucose-6-Phosphate dehydrogenase impairs cardiac contractile performance and efficiency in conscious dogs. *Circulation*. 2011 Nov;124(21Suppl1):A12821. Available from: http://circ.ahajournals.org/cgi/content/meeting_abstract/124/21_MeetingAbstracts/A12821

Weber DS, Jadhav R, Dodd T, Smith E, Bennet JR, Rocic P. Sustained activation of p38 MAPK and MMP2 and 9 exacerbate neointima formation following vascular injury in metabolic syndrome rat. *FASEB J*. 2012;26:866.20.

Xu N, Cioffi DL, Wang X, Cioffi EA, Alexeyev M, Stevens T. Orail is a critical determinant of sodium influx through store operated calcium entry channels. *Am J Respir Crit Care Med*. 2012 May 1;185:A5510. Available from: http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A5510

III. PUBLISHED BOOKS

IV. INVITED PRESENTATIONS

Gerthoffer WT. Invited speaker. MicroRNAs and smooth muscle phenotype. Department of Cell Physiology and Molecular Biophysics, Texas Tech University; 2011 Oct 13; Lubbock, TX.

Gerthoffer WT. Invited speaker. MicroRNAs and smooth muscle phenotype. Stitzel Lecturer, West Virginia University; 2011 Oct 26; Morgantown, WV.

Gerthoffer WT. Invited speaker. Noncoding RNAs in normal functions and lung pathology. American Thoracic Symposium - Epigenetic targets for novel therapy of lung diseases; 2012 May 23; San Francisco, CA.

Gupte SA. Invited speaker. G6PD and stem cells in vascular biology. Science Department, Berry College; 2012 Jan 31; Rome, GA.

Honkanen RE. Invited speaker. PP5 an often overlooked PPP-family phosphatase. FASEB Summer Research Conferences, Protein phosphatases; 2012 Jul 16; Snowmass, CO.

LeClaire LL. Invited speaker. Phosphorylation of the Arp2/3 Complex: conformational changes and regulation in migrating breast cancer cells. 1st Annual Cancer Research Symposium, Mitchell Cancer Institute; 2011 Oct 24; Mobile, AL.

LeClaire LL. Invited speaker. Controlling cell migration by phosphorylation of the arp2/3 complex. Mitchell Cancer Institute Seminar. 2012 Mar 13; Mobile, AL.

LeClaire LL, Narayanan A, Jacobson M, Barber DL. Invited speakers. Arp2/3 Complex phosphorylation: conformation changes and regulation in migrating cells. 2011 Annual Meeting of the American Society for Cell Biology; 2011 Dec 6; Denver, CO.

Lim ST. Invited speaker. Nuclear role of FAK in inflammation signaling. FASEB Summer Research Conferences, Tyrosine Kinase Signaling in Cancer, Disease & Development; 2012 Jul 24; Snowmass, CO.

Rocic P. Invited speaker. Redox-sensitive pathways in coronary collateral growth. American Heart Association Scientific Sessions; 2011 Nov 13; Orlando, FL.

V. NATIONAL PROFESSIONAL RECOGNITION

Cioffi DL: Reviewer, *American Journal of Physiology-Cell Physiology*, *American Journal of Physiology-Lung Cellular and Molecular Physiology*.

Gerthoffer WT: Editorial Board Member, *American Journal of Physiology*, *Cell Physiology*; Editorial Board Member, *American Journal of Physiology, Lung Cell and Molecular*; Editorial Board Member, *Cell Health and Cytoskeleton*; Associate Editor, *Comprehensive Physiology, Respiratory Physiology*; Chairman, American Thoracic Society, Planning Committee of the RSF Assembly; Reviewer NIH, VCMB study section (ad hoc); Reviewer NIH Surgical Sciences, Biomedical Imaging, and Bioengineering SEP (ad hoc).

Gupte SA: Editorial Board Member, *American Journal of Physiology, Heart and Circulatory*; Associate Editor, *World Research Journal of Biochemistry*; Guest Editor, *Antioxidant & Redox Signaling*; Study Section, Italian Health Ministry, Government of Italy; Swiss Science Foundation and Government of Switzerland.

Honkanen RE: Editorial Board Member, *The Open Enzyme Inhibition Journal*; NIH ZRG1 BST-J51 Review Group Panel Member, NIH Roadmap Initiative (Assay Development for High Throughput Molecular Screening).

Lim ST: Associate Editor, *World Research Journal of Cell Biology*.

Rocic P: Editorial Board Member, *American Journal of Physiology, Heart and Circulatory Physiology, Microcirculation, Vascular Pharmacology, Atherosclerosis, Life Sciences*; Peer Review Committee Member - Circulation Research, Microcirculation, *American Journal of Physiology: Heart and Circulatory Physiology, Microcirculation, Vascular Pharmacology, Atherosclerosis, Life Sciences*.

VI. BRIEF SUMMARY OF ACTIVITIES AND PROGRESS

Recruitment of new faculty to the department has continued in 2012. A successful joint search conducted with the Department of Physiology resulted in hiring of Dr. Steve Lim, who joined the faculty in January 2012. Dr. Lim trained at the University of Alabama, Birmingham and was a postdoctoral fellow in the Department of Reproductive Medicine, UC San Diego prior to joining the University of South Alabama. His expertise in molecular biology of the focal adhesion kinase builds on existing research expertise on cytoskeletal proteins in the department and in the College of Medicine. Since joining the department, he obtained national funding from the American Heart Association for his studies of focal adhesion kinase in the cardiovascular system. Dr. Lim also has interests in pursuing some novel functions of focal adhesion kinase in studies of cancer metastasis. His cancer-related interests add to a growing focus on cancer molecular cell biology already under way in the Honkanen and LeClaire labs.

Education activities in the department have focused on revising the medical curriculum and continuing to contribute to graduate education. Several faculty members, including the chair, have participated in planning and implementing a major revision of the first year medical course. The faculty have added case-based lectures and self-directed modules and team-based learning lessons to the Foundations of Human Health module. The faculty all contributed to multiple IDL graduate courses and participate in the Lung Biology, Vascular Biology, Cancer Biology and Cell and Molecular Biology tracks of the graduate program. Five fourth year graduate students and two third year students are training with department faculty members (Gerthoffer, S. Gupte, Rocic, Cioffi). One student, Tracy Dodd, finished her degree and is a postdoctoral fellow with Dr. Patricia Molina, Louisiana State University. The department also contributed to biomedical science education by hosting sophomore medical students and a USA undergraduate in the College of Medicine and UCUR summer research programs respectively.

Research funding remains strong and all labs are active and productive. Three of the four junior faculty members direct active labs funded by NIH grants. Dr. Cioffi recently won a second NIH grant to support novel work on endothelial cell calcium signaling. A fourth junior faculty member, Dr. Lim, is funded by a Scientist Development Grant from AHA National Center. The senior faculty R. Honkanen (protein phosphatase-5) and W. Gerthoffer (small heat shock proteins, miRNAs) continue to be supported by multiple NIH grants. Dr. Honkanen was awarded a prestigious NIH Director's Transformative Research Project Award. Two fellowships from the American Heart Association were awarded to department trainees. Dr. A. Vasauskas working with Dr. D. Cioffi is supported by an NIH NRSA postdoctoral fellowship. Rebecca Hutcheson (GSII) training with Dr. Rocic is supported by an NIH predoctoral fellowship.

In addition, new grant applications from every faculty member either have been submitted, or are in development. The faculty funding, publication rate and impact are nationally competitive on a per capita basis. The faculty have significant impact on their respective fields as demonstrated by publication of invited reviews and invitations to speak at symposia at national meetings (Gerthoffer, Rocic, Honkanen, LeClaire) and at other universities. The faculty also contributes significantly to regional and national peer review, serving peer review committees for AHA, the NIH and American Cancer Society as well as ad hoc service for international granting agencies. Several faculty members serve on journal editorial boards and others contribute regularly as journal reviewers. With a solid base of funded, productive biomedical researchers, the department anticipates continued growth in scholarship and impact on our respective scientific fields.