

2009-2010
Summary of Scholarly Activities
Department of Biochemistry & Molecular Biology

I. PUBLISHED JOURNAL ARTICLES, BOOK CHAPTERS, AND PATENTS

Carrão AC, Chilian WM, Yun J, Kolz C, Rocic P, Lehmann K, van den Wijngaard JP, van Horssen P, Spaan JA, Ohanyan V, Pung YF, Buschmann I. Stimulation of coronary collateral growth by granulocyte stimulating factor. Role of reactive oxygen species. *Arterioscler Thromb Vasc Biol* 2009 Nov;29(11):1817-22.

Cioffi DL, Barry C, Stevens T. Store-operated calcium entry channels in pulmonary endothelium: the emerging story of TRPCS and Orai1. *Adv Exp Med Biol* 2010;661:137-54.

Cioffi DL, Wu S, Stevens T. Lung endothelial phenotypes: insights derived from the systematic study of calcium channels. In: Voelkel NF, Rounds S, editors. *The pulmonary endothelium; function in health and disease*. Hoboken, NJ:Wiley-Blackwell; 2009. Chapter 9. p. 129-42.

Gupte RS, Rawat DK, Chettimada S, Cioffi DL, Wolin MS, Gerthoffer WT, McMurtry IF, Gupte SA. Activation of glucose-6-phosphate dehydrogenase promotes acute hypoxic pulmonary artery contraction. *J Biol Chem* 2010 Jun 18;285(25):19561-71.

Gupte SA. Targeting the pentose phosphate pathway in syndrome X-related cardiovascular complications. *Drug Dev Res* 2010 May 1;71(3):161-7.

Gupte SA, Labinsky N, Gupte R, Csiszar A, Ungvari A, Edwards JG. Role of NAD(P)H oxidase in superoxide generation and endothelial dysfunction in Goto-Kakizaki aGK rats as a model of nonobese NIDDM. *PLoS One* [Internet] 2010 Jul 26;5(7):e11800. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2909910/pdf/pone.0011800.pdf>

Harpen M, Barik T, Musiyenko A, Barik S. Mutational analysis reveals a non-contractile but interactive role of actin and profilin in viral RNA-dependent RNA synthesis. *J Virol* 2009 Nov;83(21):10869-76.

Hinoki A, Kimura K, Higuchi S, Eguchi K, Takaguri A, Ishimaru K, Frank GD, Gerthoffer WT, Sommerville LJ, Autieri MV, Eguchi S. p 21-activated kinase 1 participates in vascular remodeling in vitro and in vivo. *Hypertension* 2010 Jan;55(1):161-5.

Kim M, Park SW, Kim M, Chen SW, Gerthoffer WT, D'Agati VD, Lee HT. Selective renal over-expression of human heat shock protein 27 reduces renal ischemia-reperfusion injury in mice. *Am J Physiol Renal Physiol* 2010 Aug;299(2):F347-58.

Mazumder B, Li X, Barik S. Translation control: a multifaceted regulator of inflammatory response. *J Immunol* 2010 Apr 1;184(7):3311-9.

Musiyenko A, Correa L, Stock N, Hutchinson JH, Lorrain DS, Bain G, Evans JF, Barik S. A novel 5-lipoxygenase-activating protein inhibitor, AM679, reduces inflammation in the respiratory syncytial virus-infected mouse eye. *Clin Vaccine Immunol* 2009 Nov;16(11):1654-9.

Rocic B, Bajuk NB, Rocic P, Weber DS, Boras J, Lovrencic MV. Comparison of antihyperglycemic effects of creatine and metformin in type II diabetic patients. *Clin Invest Med* 2009 Dec 1;32(6):E322.

Rocic P. Differential phosphoinositide 3-kinase signaling: implications for PTCA? *Am J Physiol Heart Circ Physiol* 2009 Dec;297(6):H1970-1.

Swedan S, Musiyenko A, Barik S. Respiratory syncytial virus nonstructural proteins decrease multiple members of the cellular interferon pathways. *J Virol* 2009 Oct;83(19):9682-93.

Swingle MS, Amable L, Lawhorn BG, Buck SB, Burke CP, Ratti P, Fischer KL, Boger DL, Honkanen RE. Structure-activity relationship studies of Fostriecin, Cytostatin and key analogues, with PP1, PP2A, PP5, and (β 12- β 13)-chimeras (PP1/PP2A and PP5/PP2A) provide further insight into inhibitory actions of Fostriecin family inhibitors. *J Pharmacol Exp Ther* 2009 Oct;331(1):45-53.

Wolin MS, Gupte SA, Mingone CJ, Neo BH, Gao Q, Ahmad M. Redox regulation of responses to hypoxia and NO-cGMP signaling in pulmonary vascular pathophysiology. *Ann N Y Acad Sci* 2010 Aug;1203:126-32.

Wolin MS, Gupte SA, Neo BH, Gao Q, Ahmad M. Oxidant-redox regulation of pulmonary vascular responses to hypoxia and nitric oxide-cGMP signaling. *Cardiol Rev* 2010 Mar-Apr;18(2):89-93.

II. PUBLISHED ABSTRACTS

Barry CF, Wu S, Cioffi DL, Stevens T. Disruption of the constitutive spectrin-actin interaction induces inter-endothelial cell gap formation. *Am J Respir Crit Care Med* 2010 May;181:A3428. Available from: http://ajrccm.atsjournals.org/cgi/reprint/181/1_MeetingAbstracts/A3428

Chen H, Cioffi DL, Alexeyev MF, Wu S, Stevens T. Contribution of Orail to a Ca^{2+} selective store-operated current, I_{soc} , in pulmonary artery endothelial cells. *Am J Respir Crit Care Med* 2010 May;181:A3424. Available from: http://ajrccm.atsjournals.org/cgi/reprint/181/1_MeetingAbstracts/A3424

Chettimada S, Oka M, McMurtry IF, Gupte SA. Role of glucose-6-phosphate dehydrogenase (G6PD) in chronic hypoxia-induced pulmonary hypertension. *FASEB J* 2010 Apr;24:1023.2.

Cioffi DL, Cioffi EA. Glycomorphology of the pulmonary vasculature: endothelial cell glycocalyx and endothelial barrier function. *Am J Respir Crit Care Med* 2010 May;181:A1041. Available from: http://ajrccm.atsjournals.org/cgi/reprint/181/1_MeetingAbstracts/A1041

Dodd TY, Jadhav R, Smith E, Rocic P. p38 MAPK-dependent regulation of MMPs during coronary collateral growth. *FASEB J* 2010 Apr;24:599.16.

Grankvist N, Honkanen RE, Ortsater H, Sjöholm A. Serine/threonine phosphatase 5 is involved in the regulation of fatty acid-induced Beta cell apoptosis. 45th Annual Meeting of the European Association for the Study of Diabetes, 2009 Sept 29-Oct 2; Vienna Austria. p. 151. Poster 537. Abstract 387.

Gupte RS, Kurebayashi N, Gupte SA. Glucose-6-phosphate dehydrogenase interacts with Cav1.2 and regulates $[Ca^{2+}]_i$ in coronary artery smooth muscle. *FASEB J* 2010 Apr;24:lb549.

Honkanen RE, Bonness K, Huang X, Dean N. Studies into the antitumor activity of fostriecin reveal a critical role for ser/thr protein phosphatase 4 (PP4) in the regulation of cell cycle progression. *FASEB Summer Research Conference 2010 Jul 18-23; Steamboat, CO.* p. 83. Poster P20.

Ochi R, Gupte RS, Murayama T, Kurebayashi N, Gupte SA. Apocynin inhibits and its removal augments L-type Ca^{2+} currents in coronary artery smooth muscle cells and ventricular myocytes. *FASEB J* 2010 Apr;24:595.7.

Ochi R, Gupte RS, Murayama T, Kurebayashi N, Gupte SA. Apocynin reversibly inhibits L-type Ca^{2+} channel current. involvement of reactive oxygen species. Biophysical Society 54th Annual Meeting 2010 Feb 19 – 24; San Francisco, CA. p. 697. Poster B578.

Ortsater H, Fransson L, Grankvist N, Honkanen, RE, Sjöholm A. Serine/threonine protein phosphatase 5 mediates dexamethasone-induced beta cell death through its modulation of p38 MAPK phosphorylation. 45th Annual Meeting of the European Association for the Study of Diabetes, 2009 Sept 29-Oct 2; Vienna Austria. p. 151. Poster 535.

Rawat DK, Gupte RS, Chettimada S, McMurtry IF, Gupte SA. Activation of glucose-6-phosphate dehydrogenase promotes acute hypoxic pulmonary artery contraction. FASEB J 2010 Apr;24:795.6.

Torres RA, Drake DA, Solodushko V, Jadhav R, Smith ES, Rocic P, Weber DS. Slingshot-isoform specific regulation of cofilin activation during VSMC migration and neointima formation following vascular injury. FASEB J 2010 Apr;24:790.7.

Villalta PC, Rocic P, Townsley MI. Impact of cyclic strain on integrin expression in rat pulmonary microvascular endothelial cells. FASEB J 2010 Apr;24:797.1.

Volmar CH, Saldanha SA, Honkanen R, Swingle M, Chase P, Eberhart C, Hodder P. Identification of protein phosphatase inhibitors by fluorescence-based biochemical ultra high throughput screening assay. SBS 16th Annual Conference and Exhibition 2010 Apr 11-15; Phoenix, AZ. Poster B283.

III. PUBLISHED BOOKS

IV. INVITED PRESENTATIONS

Barik S. Invited speaker. Lung-pathogen relationships: mechanisms of defense and survival. Cleveland State University; 2010 Mar 25; Cleveland, OH.

Gerthoffer W. Invited speaker. MicroRNAs in smooth muscle remodeling. Whitaker Cardiovascular Institute, Boston University; 2010 Feb 16; Boston, MA.

Gerthoffer W. Invited speaker. Novel insights into the pathogenesis of pulmonary arterial hypertension. Therapeutic Potential in PAH Symposium; American Thoracic Society 2010 Conference; 2010 May 17; New Orleans, LA.

Gerthoffer W. Invited speaker. The interplay of lung inflammation, lung remodeling, and lung function. American Thoracic Society 2010 Conference; 2010 May 17; New Orleans, LA.

Honkanen R. Invited speaker. Studies into the antitumor activity of fostriecin and PP2A reveal a critical role for both PP2A and PP4 in the regulation of cell cycle progression. FASEB Summer Research Conferences; 2010 Jul 20; Steamboat, CO.

Rocic P. Invited speaker. p38 MAPK-dependent regulation of MMPs during coronary collateral growth. Experimental Biology 2010; 2010 Apr 25; Anaheim, CA.

V. NATIONAL PROFESSIONAL RECOGNITION

Sailen Barik, Permanent Member, Standing NIH Study Section: Virology-B, 2006-2010; Associate Editor, *BMC Microbiology*.

William T. Gerthoffer, 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, LCMI study section (ad hoc), RC4 Grants.

Sachin A. Gupte, Editorial Board Member, *American Journal of Physiology, Heart and Circulatory Physiology* and *Antioxidant & Redox Signaling*; Guest Editor, *Antioxidant & Redox Signaling*.

Richard E. Honkanen, FASEB Summer Research Conference, Protein Phosphatases, invited speaker, Named co-organizer for the 2012 meeting; Review Group Panel Member, NIH ZRG1 BST-J51 NIH Roadmap Initiative (Assay Development for High Throughput Molecular Screening); Editorial Board Member, *The Open Enzyme Inhibition Journal*.

Petra Rocic, Editorial Board Member, *American Journal of Physiology: Heart and Circulatory Physiology*; Editorial Board Member, *Microcirculation*; Peer-Review Group, American Heart Association, National.

VI. BRIEF SUMMARY OF ACTIVITIES AND PROGRESS

The department has undergone significant changes in personnel in the past year. Dr. Roger Lane announced his retirement after 32 years of service to the department during which time he served as a researcher and highly respected medical educator. Dr. Lane will continue in a limited role as a lecturer in Medical Biochemistry. Another senior faculty member, Dr. Sailen Barik, has relocated to Cleveland State University to direct the Center for Gene Regulation in Health and Disease. Dr. Barik served as a productive, highly regarded virologist and educator for many years. His contribution to the department research enterprise has been substantial and he will be missed. Turnover of existing personnel has been balanced in the past three years by successful searches to fill

four vacant faculty positions. The most recent recruit, Dr. Lawrence LeClaire, will join the faculty in 2011, coming from the Department of Cell and Tissue Biology, UCSF. He brings expertise in protein biochemistry with emphasis on the actin cytoskeleton. A new postdoctoral fellow, Dr. Sachindra Joshi, joined the Gerthoffer lab where he conducts research on the role of miRNAs in smooth muscle differentiation. Dr. Joshi completed his doctoral work at Bowling Green State University in 2009 where he studied proteins that regulate estrogen response elements.

Education activities in the department are focused on updating the medical biochemistry course and expanding the scope and role of the department in graduate education. Medical Biochemistry is in transition to a format more consistent with current trends in medical education. Key changes include more case-based approaches, self-directed study of clinical problems and use of the student-response system for in-class assessment of student learning. In addition to our role in undergraduate medical education the faculty all contribute to multiple IDL and departmental graduate courses. Two senior graduate students, Joel Andrews and Samer Swedan, graduated in 2010. Dr. Andrews is a postdoctoral fellow at the Mitchell Cancer Institute and Dr. Swedan is an Assistant Professor of Medical Laboratory Sciences, at the College of Applied Medical Sciences, Jordan University of Science and Technology. Five second year graduate students and two first year students are training with department faculty members (Gerthoffer, Gupte, Rocic, Cioffi).

Teaching faculty also contribute to a summer biochemistry course in phase II of the DREAM program which is directed by Dr. Gerthoffer. The program targets disadvantaged undergraduate students interested in a medical career. Drs. Cioffi, Gerthoffer, Gupte, Honkanen, and Rocic contributed lectures. The department also contributes to biomedical science education by hosting freshman and sophomore medical students and USA undergraduates in the College of Medicine, UCUR and Center for Healthy Communities summer research programs.

The level of research activity and research funding remains robust. The junior faculty all manage active labs funded by NIH grants. The senior faculty R. Honkanen (Protein phosphatase-5) and W. Gerthoffer (small heat shock proteins) continue to be supported by NIH grants. Dr. Rocic succeeded in obtaining two supplements through ARRA funding of NIH programs, one for support of a graduate student, Ms Tracy Dodd. In addition, new grant applications from every faculty member have either been submitted, or are in development. The number of research awards has increased from 13 funded projects in 2008-2009 to 17 in 2009-2010. The faculty publication rate and impact is similar to the previous year, and is appropriate for a small size department. A high level of scholarly activity is evidenced by invited presentations at national and international scientific conferences, participation on national and regional peer review committees and memberships on journal editorial boards.

With continued expansion and development of recently hired faculty members the department anticipates further positive trends in medical and graduate education and continued growth in the scope and impact of scholarly activity in the near future.