

**2011-2012**  
**Summary of Scholarly Activities**  
**Department of Pharmacology**

**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.

Al-Mehdi AB, Pastukh VM, Swiger BM, Reed DJ, Patel MR, Bardwell GC, Pastukh VV, Alexeyev MF, Gillespie MN. Perinuclear mitochondrial clustering creates an oxidant-rich nuclear domain required for hypoxia-induced transcription. *Sci Signal*. 2012 Jul 3;5(231):ra47.

Ata H, Shrestha D, Oka M, Ochi R, Jong CJ, Gebb S, Benjamin J, Schaffer S, Hobart HH, Downey J, McMurtry I, Gupte R. Down-regulation of replication factor C-40 (RFC40) causes chromosomal missegregation in neonatal and hypertrophic adult rat cardiac myocytes. *PLoS ONE* 2012;7(6):3. e39009. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3375256/pdf/pone.0039009.pdf>

Bailey SW, Ayling JE, Offer T, Lenton KJ. Methods and compositions containing natural folates for protecting against radiation damage. Chinese patent #ZL200680022576.1, 2012 Mar 21.

Boilson A, Staines A, Kelleher CC, Daly L, Shirley I, Shrivastava A, Bailey SW, Alverson PB, Ayling JE, Parle McDermott A, Maccooey A, Scott JM, Sweeney MR. Unmetabolized folic acid prevalence is widespread in the older Irish population despite the lack of a mandatory fortification program. *Am J Clin Nutr*. 2012 Sep;96(3):613-21.

Chouteau JM, Obiako B, Gorodnya OM, Pastukh VM, Ruchko MV, Wright AJ, Wilson GL, Gillespie MN. Mitochondrial DNA integrity may be a determinant of endothelial barrier properties in oxidant-challenged rat lungs. *Am J Physiol Lung Cell Mol Physiol*. 2011 Dec;301(6):L892-8.

Cioffi DL, Pandey S, Alvarez DE, 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.

Clark DW, Phang T, Edwards MG, Geraci MW, Gillespie MN. Promoter G-quadruplex sequences are targets for base oxidation and strand cleavage during hypoxia-induced transcription. *Free Radic Biol Med*. 2012 Jul 1;53(1):51-9.

Feinstein WP, Zhu B, Leavesley SJ, Sayner SL, Rich TC. Assessment of cellular mechanisms contributing to cAMP compartmentalization in pulmonary microvascular endothelial cells. *Am J Physiol Cell Physiol*. 2012 Mar;302(6):C839-52.

Gairhe S, Bauer NN, Gebb SA, McMurtry I. Myoendothelial gap junctional signaling induces differentiation of pulmonary arterial smooth muscle cells. *Am J Physiol Lung Cell Mol Physiol*. 2011 Oct;301(4):L527-35.

Ito T, Schaffer SW, Azuma J. The potential usefulness of taurine on diabetes mellitus and its complications. *Amino Acids*. 2012 May;42(5):1529-39.

Jong CJ, Azuma J, Schaffer S. Mechanism underlying the antioxidant activity of taurine: prevention of mitochondrial oxidant production. *Amino Acids*. 2012 Jun;42(6):2223-32.

Leavesley SJ, Annamdevula N, Boni J, Stocker S, Grant K, Troyanovsky B, Rich TC, Alvarez DF. Hyperspectral imaging microscopy for identification and quantitative analysis of fluorescently-labeled cells in highly autofluorescent tissue. *J Biophotonics*. 2012 Jan;5(1):67-84.

Ochoa CD, Alexeyev M, Pastukh V, Balczon R, Stevens T. *Pseudomonas aeruginosa* exotoxin Y is a promiscuous cyclase that increases endothelial tau phosphorylation and permeability. *J Biol Chem*. 2012 Jul 20;287(30):25407-18.

Ochoa CD, Stevens T. Studies on the cell biology of interendothelial cell gaps. *Am J Physiol Lung Cell Mol Physiol*. 2012 Feb;302(3):L275-86.

Rabiyousefi M, Soroosh P, Satoh K, Date F, Ishii N, Yamashita M, Oka M, McMurtry IE, Shimokawa H, Nose M, Sugamura K, Ono M. Indispensable roles of OX40L-derived signal and epistatic genetic effect in immune-mediated pathogenesis of spontaneous pulmonary hypertension. *BMC Immunol*. 2011 Dec 15;12:67-79.

Samapati R, Yang Y, Yin J, Stoerger C, Arenz C, Dietrich A, Gudermann T, Adam D, Wu S, Freichel M, Flockerzi V, Uhlig S, Kuebler WM. Lung endothelial Ca<sup>2+</sup> and permeability response to platelet-activating factor is mediated by acid sphingomyelinase and transient receptor potential classical 6. *Am J Respir Crit Care Med*. 2012 Jan 15;185(2):160-70.

Stevens T. Functional and molecular heterogeneity of pulmonary endothelial cells. *Proc Am Thorac Soc*. 2011 Nov;8(6):453-7.

Weir EK, Wagner WW Jr, Archer SL. Lofty goals at high altitude: The Grover Conference, 1984-2011. *Pulm Circ.* 2011 Oct-Dec 2011;1(4):501-7. Available from: <http://ncbi.nlm.nih.gov/pmc/articles/pmc3329081>

Xin W, Yang X, Rich TC, Krieg T, Barrington R, Cohen MV, Downey JM. All preconditioning-related G protein-coupled receptors can be demonstrated in the rabbit cardiomyocyte. *J Cardiovasc Pharmacol Ther.* 2012 Jun;17(2):190-8.

Zeng H, Pappas C, Belser JA, Houser KV, Zhong W, Wadford DA, Stevens T, Balczon R, Katz JM, Tumpey TM. Human pulmonary microvascular endothelial cells support productive replication of highly pathogenic avian influenza viruses: possible involvement in the pathogenesis of human H5N1 virus infection. *J Virol.* 2012 Jan;86(2):667-78.

## II. PUBLISHED ABSTRACTS

Alzoubi A, Almalouf P, Toba M, O'Neill KD, Matsumoto Y, Oka M, McMurtry IF, Stevens T. Trpc4 channels and pulmonary arterial hypertension: observations from study of trpc4 knockout rats. *Am J Respir Crit Care Med.* 2012 May 1;185:A3437. Available from: [http://ajrccm.atsjournals.org/cgi/reprint/185/1\\_MeetingAbstracts/A3437](http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A3437)

Alzoubi A, Toba M, Abe K, Bauer NN, Fagan K, McMurtry IF, Oka M. Dehydroepiandrosterone restores right ventricular structure and function in a pre-clinical model of severe pulmonary arterial hypertension. *Am J Respir Crit Care Med* 2012. 185:A3449. Available from: [http://ajrccm.atsjournals.org/cgi/reprint/185/1\\_MeetingAbstracts/A3449](http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A3449)

Bailey SW, Ayling JE. Elevation of folate status in humans by 5-methyl-6S-tetrahydrofolate. *FASEB J.* 2012;26:1020.4.

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

Gairhe S, Alzoubi A, Toba M, Oka M, McMurtry IF. Effect of dehydroepiandrosterone on the expression of sphingosine kinases in pulmonary arteries of Sugen hypoxia rat model of pulmonary arterial hypertension. *Am J Respir Crit Care Med.* 2012 May 1;185:A4777. Available from: [http://ajrccm.atsjournals.org/cgi/reprint/185/1\\_MeetingAbstracts/A4777](http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A4777)

Gairhe S, Oka M, McMurtry IF. Pulmonary arterial expression of sphingosine kinases is markedly increased in pulmonary arterial hypertension. *Am J Respir Crit Care Med.* 2012 May 1; 185:A4752. Available from: [http://ajrccm.atsjournals.org/cgi/reprint/185/1\\_MeetingAbstracts/A4752](http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A4752)

Hargett LA, Brown L, Sayner S, Bauer NN. Microparticles from pulmonary microvascular endothelial cells contain cyclic AMP. *Am J Resp Crit Care Med*. 2012 May 1;185A4819. Available from: [http://ajrccm.atsjournals.org/cgi/reprint/185/1\\_MeetingAbstracts/A4819](http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A4819)

Hill JK, Mulekar S, Pastukh VM, Gillespie MN. Mitochondrial DNA damage-associated molecular patterns are released in response to oxidant stress in rat pulmonary artery endothelial cells. *FASEB J*. 2012;26:1130.12.

Hill JK, Kua J, Obiako B, Pastukh VM, Gillespie MN. Mitochondrial DNA damage-associated molecular patterns released in response to *P. aeruginosa* contribute to endothelial barrier dysfunction in perfused rat lungs. *Am J Respir Crit Care Med*. 2012 May 1; 185:A1866. Available from: [http://ajrccm.atsjournals.org/cgi/reprint/185/1\\_MeetingAbstracts/A1866](http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A1866)

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/185/1MeetingAbstracts/A4772>

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](http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A3407)

O'Neill K, Reece A, Alzoubi A, Toba M, Oka M, McMurtry IF, Fagan KA. Blockade of either alpha-5 and beta-1 integrin inhibits pulmonary arterial contraction: possible role in PAH. *Am J Respir Crit Care Med*. 2012 May 1;185:A4829. Available from: [http://ajrccm.atsjournals.org/cgi/reprint/185/1\\_MeetingAbstracts/A4829](http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A4829)

Pastukh VM, Bardwell GC, Patel M, Al-Mehdi AB, Gillespie MN. The DNA glycosylase Ogg1 is required for hypoxia-induced activation of VEGF transcription in pulmonary artery endothelial cells (PAECs). *FASEB J*. 2012 Apr;26:699.8.

Platt TA, Oka M, McMurtry IF. Mechanism of contraction of hypoxia-induced hypertensive rat pulmonary arteries. *Am J Respir Crit Care Med*. 2012 May 1; 185:A4769. Available from: [http://ajrccm.atsjournals.org/cgi/reprint/185/1\\_MeetingAbstracts/A4769](http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A4769)

Ruchko MV, Gorodnya OM, Pastukh VM. Mitochondrial biogenesis in hypoxic rat pulmonary artery endothelial cells: possible involvement of DNA oxidation. *FASEB J*. 2012;26:699.9.

Samapati R, Yang Y, Yin J, Stoerger C, Arenz C, Dietrich A, Adam D, Wu S, Freichel M, Flockerzi V, Uhlig S, Kuebler WM. Lung endothelial Ca<sup>2+</sup> and permeability response to PAF is mediated by TRPC6. *FASEB J*. 2012 Apr;26:1056.6.

Toba M, Alzoubi A, Abe K, Urakami T, Komatsu M, Matsumoto Y, Alvarez D, Jarvinen TAH, Mann D, Ruoslahti E, McMurtry IF, Oka M. The cell-penetrating homing peptide CAR selectively enhances pulmonary effects of systemically co-administered vasodilators in a preclinical model of severe pulmonary arterial hypertension. *Am J Respir Crit Care Med*. 2012 May 1;185:A1239. Available from: [http://ajrccm.atsjournals.org/cgi/reprint/185/1\\_MeetingAbstracts/A1239](http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A1239)

Toba M, Alzoubi A, O'Neill K, Gairhe S, Matsumoto Y, Abe K, McMurtry IF, Oka M. Time-course of hemodynamic and histological progression in SU5416/hypoxia/normoxia-exposed pulmonary arterial hypertensive rats. *Am J Respir Crit Care Med* 2012 May 1;185:A1244. Available from: [http://ajrccm.atsjournals.org/cgi/reprint/185/1\\_MeetingAbstracts/A1244](http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A1244)

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

Wang X, Chen H, Wu S, Cioffi DL. Role of the TRPC4 proline rich region in regulation of the endothelial store-operated calcium entry. *FASEB J*. 2012;26:1130.8.

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](http://ajrccm.atsjournals.org/cgi/reprint/185/1_MeetingAbstracts/A5510)

### III. PUBLISHED BOOKS

### IV. INVITED PRESENTATIONS

Bailey SW, Ayling JE. Invited speaker. Rapid folate repletion as an additional option for prevention of birth defects. *Advances and Controversies in B-Vitamins and Choline Annual Conference 2012 Mar 7; Leipzig, Germany.*

Bauer N. Invited speaker. Big signals come in small packages: the role of microparticles in mediating PAH. *American Thoracic Society International Meeting; 2012 May 20; San Francisco, CA.*

Gillespie MN. Invited speaker. Endothelial cell responses to oxidant stress; a tale of two genomes. *University of Pennsylvania, Institute of Environmental Medicine; 2012 Jun 29; Philadelphia, PA.*

Schaffer SW. Invited speaker. The role of the giant protein titin in systolic and diastolic dysfunction. *Fresenius Kabi Expert Meeting Cardiology; 2012 Sep 12; Mainz, Germany.*

Wu S. Invited speaker. The  $\alpha_{1G}$  T-type  $Ca^{2+}$  channel and lung endothelial cell proinflammatory phenotype. The University of Texas Health Science Center; 2011 Nov 14; Tyler, TX.

## V. NATIONAL PROFESSIONAL RECOGNITION

Ayling JE: Peer Reviewer, *American Journal of Clinical Nutrition*, *Photochemistry*, *Photobio*, *PLoS One*, *Journal of Nutrition*.

Bauer N: Study Sections Member for American Heart Association, American Lung Association, National Institutes of Health (NHLBI); Peer Reviewer, *American Journal of Physiology Lung Cellular and Molecular Physiology*, *Physiology Reviews*, and *PLoS One*; Member, Nominating Committee, Gulf Coast Physiological Society; Member, Programming Committee, Scientific Symposium Organizer, Poster Session Facilitator, American Thoracic Society.

Chinkers M: Peer reviewer, *American Chemical Society Neuroscience*, *Acta Biochimica et Biophysica Molecular Cellular Research*.

Cioffi EA: Invited participant, Gulf of Mexico Alliance (GOMA), Mercury Forum; Pensacola, FL.

Gillespie MN: Editorial Board, *American Journal of Physiology, Lung Cellular and Molecular Physiology*; and *American Journal of Respiratory Cellular and Molecular Biology*. Program, Leadership, and Long Range Planning Committees, American Thoracic Society; Ad hoc member of NIH study sections (1), Special Emphasis Panel (2), RIBT (1); American Lung Association Research Peer Review Panel; AP Fishman Lecturer, University of Pennsylvania.

McMurtry IF: Study sections for grant review NHLBI Workgroup HLBP; Canadian Institutes of Health Research review. Journal editor or editorial board member Physiology Society's *Comprehensive Physiology: Topic on Pulmonary Circulation and Non-Respiratory Functions*; International Associate Editor, *Circulation Journal* Editorial Board, *American Journal of Physiology Lung*. Reviewed manuscripts for *American Journal Physiology Lung*, *American Journal of Physiology Heart, Cardiovascular Research*, *Circulation*, *European Respiratory Journal*, *Nature Medicine*. Dr. McMurtry received the 2012 ATS Assembly on Pulmonary Circulation Leadership Award at the 2012 national convention.

Rich TC: Member, American Heart Association Signaling II Peer Review Study Group. Ad hoc reviewer: National Institutes of Health ZRGI CB\_N 30 review panel. Ad hoc reviewer for: *Nature Protocols*, *Journal of Biology Chemistry*, *American Journal of Physiology – Lung Molecular Pharmacology*, and *Journal Cardiovascular Pharmacology Therapy*.

Schaffer SW: Study sections for the American Heart Association – Cardiac Bio Reg (BSci2); Section Editor, *Amino Acids*; Associate Editor, *Molecular Cellular Biochemistry*; Editorial Board, *Experimental Clinical Cardiology*; Editor of Special Addition, *Vascular Pharmacology*.

Solodushko V: Associate Editor, *BioMed Central Research Notes*, London, UK; Peer Reviewer, *BioMed Central Research Notes*, London, UK.

Stevens T: Associate Editor: *American Journal Physiology-Lung*; Program Project Grant Review: National Institutes of Health; Program Project Grant External Advisor: Medical College of Georgia and University of Pennsylvania; SEP Grant Reviewer: National Institutes of Health; Ad Hoc Reviewer, Respiratory Integrative Biology and Translational Research.

Wagner WW Jr.: Program, Leadership, and Long Range Planning Committees, American Thoracic Society; American Thoracic Society, Presenter, Robert F. Grover Prize: Jan Herget, Prague; Nominated, American Thoracic Society Treasurer, declined due to age; Manuscript reviewer for all major journals relevant to his field of research.

## **VI. BRIEF SUMMARY OF ACTIVITIES AND PROGRESS**

The Department of Pharmacology hosted visits from two scientists who participated in the Distinguished Scientist Seminar Series: Dr. Ronald L. Schnaar, Professor, Departments of Pharmacology, Molecular Science, and Neuroscience, The Johns Hopkins School of Medicine at Baltimore, MD presented a seminar entitled “Axon-myelin Interactions, Axon Stability and the Control of Axon Regeneration” on Thursday, December 8, 2011. Dr. Augustine M.K. Choi, Parker B. Francis Professor of Medicine, Harvard Medical School, Chief, Pulmonary and Critical Care Medicine, Brigham and Women’s Hospital at Boston, MA presented a seminar entitled “Autophagy: Regulation and Function of Lung Disease” on Thursday, April 19, 2012.

One student graduated from the Department of Pharmacology and the Center for Lung Biology. Dr. Christiaan D. Ochoa’s defense was on May 31, 2012. His dissertation was entitled, “The Microtubule-associated Proteins Tau and MAP6 in Endothelial Function.” Dr. Ochoa is a Medical Resident in the Physician Scientist Training Program at the University of Texas Southwestern Medical Center in Dallas, TX. Dr. Troy Stevens served as his major professor.

Dr. Troy Stevens and his colleagues in the Center for Lung Biology received the third consecutive competing renewal of their NIH Program Project Grant entitled “Lung Endothelial Cell Heterogeneity.” The program, which has generated nearly \$25M in extramural funding since its inception over 15 years ago, is focused on identifying new targets for drug action in acute lung injury and the acute respiratory distress syndrome.

Dr. Mark Gillespie is a partner in one of the first biotech companies to be launched along the Gulf Coast. The company, Exscien, led by Steve and Christine Cumbie, was recently awarded a Science and Technology Transfer (STTR) grant by the National Institutes of Health to support the development of a new drug to prevent and reverse acute lung injury. The USA College of Medicine will collaborate with Exscien in an effort to rapidly develop the treatments. The STTR grant and Exscien are developments that emerged from an earlier funding cycle of the above-mentioned program project grant.