2010-2011 Summary of Scholarly Activities Department of Pharmacology

I. PUBLISHED JOURNAL ARTICLES, BOOK CHAPTERS, AND PATENTS

Blackman BE, Horner K, Heidmann J, Wang D, Richter W, Rich TC, Conti M. PDE4D and PDE4B function in distinct subcellular compartments in mouse embryonic fibroblasts. J Biol Chem. 2011 Apr 8;286(14):12590-601.

Erzurum S, Rounds SI, Stevens T, Aldred M, Aliotta J, Archer SL, Asosingh K, Balaban R, Bauer N, Bhattacharya J, Bogaard H, Choudhary G, Dorn GD 2nd, Dweik R, Fagan K, Fallon M, Finkel T, Geraci F, Gladwin MT, Hassoun PM, Humbert M, Kaminski N, Kawut SM, Loscalzo J, McDonald D, McMurtry IF, Newman J, Nicolls M, Rabinovitch M, Shizuru J, Oka M, Polgar P, Rodman D, Schumacker P, Stenmark K, Tuder R, Voelkel N, Sullivan E, Weinshilboum R, Yoder MC, Zhao Y, Gail D, Moore TM. Strategic plan for lung vascular research: an NHLBI-ORDR workshop report. Am J Respir Crit Care Med. 2010 Dec 15;182(12):1554-62.

Gillespie MN, Pastukh VM, Ruchko MV. Controlled DNA "damage" and repair in hypoxic signaling. Respir Physiol Neurobiol. 2010 Dec 31;174(3):244-51.

Ochoa CD, Stevens T, Balczon R. Cold exposure reveals two populations of microtubules in endothelia. Am J Physiol Lung Cell Mol Physiol. 2011 Jan;300(1):L132-8.

Parra-Bonilla G, Alvarez DF, <u>Al-Mehdi AB</u>, Alexeyev M, <u>Stevens T</u>. Critical role for lactate dehydrogenase A in aerobic glycolysis that sustains pulmonary microvascular endothelial cell proliferation. Am J Physiol Lung Cell Mol Physiol. 2010 Oct;299(4): L513-22.

Pastukh VM, Zhang L, Ruchko MV, Gorodnya O, Bardwell GC, Tuder RM, Gillespie MN. Oxidative DNA damage in lung tissue from patients with COPD is clustered in functionally significant sequences. Int J Chron Obstruct Pulmon Dis. 2011 Mar 13;6:209-17. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3107697/pdf/copd-6-209.pdf

Ruchko MV, Gorodnya OM, Zuleta A, <u>Pastukh VM</u>, <u>Gillespie MN</u>. The DNA glycosylase Ogg1 defends against oxidant-induced mtDNA damage and apoptosis in pulmonary artery endothelial cells. Free Radic Biol Med. 2011 May 1;50(9):1107-13.

Sayner SL, Balczon R, Frank DW, Cooper DM, <u>Stevens T</u>. Filamin A is a phosphorylation target of membrane but not cytosolic adenylyl cyclase activity. Am J Physiol Lung Cell Mol Physiol. 2011 Jul;301(1):L117-24.

Schaffer SW, Jong CJ. MELAS syndrome: mediated by impaired taurinomethyluridine synthesis. In: Ostadal B, Nagano M, Dhalla NS, editors. Genes and cardiovascular function. New York: Springer Science + Business Media; 2011. Part 3, p. 93-100.

Solodushko V, Alvarez DF, Viator R, Messerall T, Fouty B. Heterogeneous activation of p19Arf in pulmonary artery smooth muscle cells. Am J Physiol Lung Cell Mol Physiol. 2011 Apr;300(4):L642-7.

Solodushko V, Fouty B. The glucocorticoid receptor in retroviral infection. In: Xu K, editor. Viral gene therapy. Rijeka, Croatia: In Tech; 2011. Chapter 4, p. 73-88.

Solodushko V, Fouty B. Mifepristone increases gamma-retroviral infection efficiency by enhancing the integration of virus into the genome of infected cells. Gene Ther. 2010 Oct;17(10):1253-61.

Urakami T, Jarvinen TA, Toba M, Sawada J, Ambalavan N, Mann D, McMurtry I, Oka M, Ruoslahti E, Komatsu M. Peptide-directed highly selective targeting of pulmonary arterial hypertension. Am J Pathol. 2011 Jun;178(6):2489-95.

Xie M, Rich TC, Scheitrum C, Conti M, Richter W. Inactivation of multidrug resistance proteins disrupts both cellular extrusion and intracellular degradation of cAMP. Mol Pharmacol. 2011 Aug;80(2):281-93.

Yang X, Xin W, Yang XM, Kuno A, Rich TC, Cohen MV, Downey JM. A2B adenosine receptors inhibit superoxide production from mitochondrial complex I in rabbit cardiomyocytes via a mechanism sensitive to Pertussis toxin. Br J Pharmacol. 2011 Jul;163(5):995-1006.

Zhu B, Zhang L, Creighton J, Alexeyev M, Strada SJ, Stevens T. Protein kinase A phosphorylation of tau-serine 214 reorganizes microtubules and disrupts the endothelial cell barrier. Am J Physiol Lung Cell Mol Physiol. 2010 Oct;299(4):L493-501.

II. PUBLISHED ABSTRACTS

Al-Mehdi A, Pastukh V, Reed D, Swiger B, Bardwell G. Discrete roles of cytoplasmic and nuclear reactive oxygen species (ROS) in hypoxia-induced transcriptional regulation. Am J Respir Crit Care Med. 2011 May 1;183:A5489. Available from: http://ajrccm.atsjournals.org/content/vol183/1_MeetingAbstracts/aindex.dtl

Alzoubi A, Toba M, Abe K, <u>Bauer N</u>, Fagan KA, <u>McMurtry I</u>, Oka M. Dehydroepiandrosterone inhibits the infiltration of proliferative bone marrow-derived hematopoietic stem cells into the perivascular space of remodeled pulmonary arteries of SU5416/hypoxia/normoxia-exposed rats. Am J Respir Crit Care Med. 2011 May 1;183: A3422. Available from: http://ajrccm.atsjournals.org/content/vol183/1_Meeting Abstracts/aindex.dtl

Balczon R, Prasain N, Prater J, Alexeyev M, Zhu B, Sayner S, Frank D, Stevens T. The pseudomonas aeruginosa Exotoxin Y impairs microtubule assembly in pulmonary microvascular endothelial cells. Am J Respir Crit Care Med. 2011 May 1;183:A4180. Available from: http://ajrccm.atsjournals.org/content/vol183/1_MeetingAbstracts/aindex.dtl

<u>Bauer N</u>, Quinn B, Toba M, Abe KA, Alzoubi A, Oka M, <u>McMurtry IF</u>. Circulating microparticles as biomarkers of disease progression in a preclinical model of pulmonary arterial hypertension. Am J Respir Crit Care Med. 2011 May 1;183:A4960. Available from: http://ajrccm.atsjournals.org/content/vol183/1_MeetingAbstracts/aindex.dtl

<u>Bauer N</u>, Quinn B. Toba M, Alzoubi A, Abe K, Oka M, <u>McMurtry IF</u>. Leukocyte and endothelial microparticle phenotypes are increased across the pulmonary vascular bed in a preclinical model of severe pulmonary arterial hypertension. Am J Respir Crit Care Med. 2011 May 1;183:A4961. Available from: http://ajrccm.atsjournals.org/content/vol183/1_MeetingAbstracts/aindex.dtl

Chouteau J, Gorodnya O, Ruchko M, Obiako B, Wilson G, Gillespie MN. Novel fusion protein constructs targeting DNA repair enzymes to mitochondria protect against pseudomonas aeruginosa-induced acute lung injury in intact rats. Am J Respir Crit Care Med. 2011 May 1;183:A3763. Available from: http://ajrccm.atsjournals.org/content/vol183/1_MeetingAbstracts/aindex.dtl

<u>Cioffi EA</u>, Alvarez DF, Pyakurel S, Cioffi D. Terminal alpha-2,3-linked sialic acids are a critical determinant of pulmonary endothelial barrier integrity. Am J Respir Crit Care Med. 2011 May 1;183:A4177. Available from: http://ajrccm.atsjournals.org/content/vol183/1_MeetingAbstracts/aindex.dtl

<u>Cioffi EA</u>, Alvarez DF, Pyakurel S, Cioffi D. Terminal alpha-2,3-linked sialic acids are a critical determinant of pulmonary endothelial barrier integrity. Gordon Research Conference in Carbohydrates; 2011 Jun 20; Waterville, ME. Abstract no. 14.

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Hasoun LZ, Bailey SW, Outlaw KK, <u>Ayling JE</u>. A potential new role for the B vitamin 5-methyl-tetrahydrofolate in human skin. FASEB J. 2011;25:608.2.

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Joshi SR, Abe K, Oka M, McMurtry IF, Gerthoffer WT. MIR-145 in vascular smooth muscle phenotype in pulmonary arterial hypertension. Am J Respir Crit Care Med. 2011 May 1;183:A3448. Available from: http://ajrccm.atsjournals.org/content/vol183/1_MeetingAbstracts/aindex.dtl

Kadeba P, Chen H, <u>Wu S</u>, <u>Scammell JG</u>, Cioffi DL. Regulation of pulmonary endothelial store-operated calcium entry by FK506-binding immunophilins. Am J Respir Crit Care Med. 2011 May 1;183:A1946. Available from: http://ajrccm.atsjournals.org/content/vol183/1_MeetingAbstracts/aindex.dtl

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Parra-Bonilla G, Alexeyev M, Alvarez D, <u>Stevens T</u>. Lactate dehydrogenase-A controls pulmonary microvascular endothelial cell network formation on matrigel. Am J Respir Crit Care Med. 2011 May 1;183:A4175. Available from: http://ajrccm.atsjournals.org/content/vol183/1_MeetingAbstracts/aindex.dtl

<u>Pastukh V</u>, Reed D, Patel M, <u>Al-Mehdi AB</u>, <u>Gillespie MN</u>. Estrogen activates an oxidant-dependent signaling pathway threatening VEGF promoter integrity in pulmonary artery endothelial cells (PAECs). FASEB J. 2011;25:1034.2.

Platt TA, Oka M, McMurtry IF. Rho kinase-mediated phosphorylation of Hsp27 in hypoxia-induced hypertensive rat pulmonary arteries. Am J Respir Crit Care Med. 2011 May 1;183:A5024. Available from: http://ajrccm.atsjournals.org/content/vol183/1_MeetingAbstracts/aindex.dtl

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Sellak H, Lincoln TM, <u>Wu S</u>. Sox9 and KLF4 transcription factors antagonize β -catenin and inhibit TCF-activity in cancer cells. FASEB J. 2011;25:115.10.

Stevens T, Nickles J. Passive transfer of anoikis-resistant endothelial cells from culture media. Am J Respir Crit Care Med. 2011 May 1;183:A4196. Available from: http://ajrccm.atsjournals.org/content/vol183/1_MeetingAbstracts/aindex.dtl

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Stocker S, Leavesley SJ, Alvarez D, <u>Rich T</u>. Spectral imaging analysis methods for fluorescence microscopy. American Institute of Chemical Engineers (AIChE) National Conference; 2010 Nov 7-12; Nashville, TN. Abstract no. 5681.

Toba M, Alzoubi A, McMurtry IF, Oka M. Expression of S100a4 is markedly unregulated in the plexiform lesions in a preclinical model of severe pulmonary arterial hypertension. Am J Respir Crit Care Med. 2011 May 1;183:A4968. Available from: http://ajrccm.atsjournals.org/content/vol183/1_MeetingAbstracts/aindex.dtl

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Zhu B, Feinstein W, Rich T, Strada SJ. PKA-mediated phosphorylation and activation of cAMP-specific phosphodiesterases in pulmonary endothelial cells. FASEB J. 2011;25: 819.19.

III. PUBLISHED BOOKS

IV. INVITED PRESENTATIONS

<u>Bauer N</u>. Invited speaker. Microparticles as biomarkers and mediators in PAH. University of Illinois Institute for Personalized Respiratory Medicine; 2011 Jul 27; Chicago, IL.

<u>Cioffi EA</u>. Invited speaker. Terminal alpha-2,3-linked sialic acids are a critical determinant of pulmonary endothelial barrier integrity. Participating Investigators Meeting; Consortium for Functional Glycomics 2011, NIH Campus; 2011 Jul 27; Bethesda, MD.

McMurtry I. Invited speaker. Recent advances in mechanisms of hypoxic pulmonary vasoconstriction. American Thoracic Society International Conference 2011; 2011 May 17; Denver, CO.

McMurtry IF. Invited speaker. Rho kinase as a therapeutic target in PAH. Pfizer Novel Targets for PAH Advisory Board; 2011 Aug 25; Paris, France.

Schaffer SW. Invited speaker. Alterations in energy metabolism mediated by taurine deficiency. 12th International Congress on Amino Acids, Peptides and Proteins 2011; 2011 Aug 4; Beijing, China.

<u>Schaffer SW</u>. Invited speaker. The role of angiotensin II in pressure-mediated ischemia-reperfusion injury. International Academy of Cardiovascular Sciences 2011; 2011 May 3; Ankara, Turkey.

Stevens T. Invited speaker. Novel mechanism of endothelial barrier disruption revealed by the study of bacterial toxins. American Thoracic Society International Conference 2011; 2011 May 16; Denver, CO.

Stevens T. Invited speaker. The P. aeruginosa ExoY is an edema factor in acute lung injury. University of Alabama at Birmingham; 2011 Feb 3; Birmingham, AL.

Stevens T. Invited speaker. P. aeruginosa ExoY is an edema factor in acute lung injury. Rush Medical College; 2011 Mar 9; Chicago, IL.

Stevens T. Invited speaker. Functional and molecular heterogeneity of pulmonary endothelial cells. Trans-Atlantic Airway Conference; 2011 Jan 19; Lucerne, Switzerland.

<u>Zhu B.</u> Invited speaker. PKA-mediated phosphorylation and activation of cAMP-specific phosphodiesterases in pulmonary endothelial cells. Experimental Biology 2011; 2011 Apr 11; Washington, DC.

Zhu B. Invited speaker. Targeting signal compartmentalization and enzyme allostery for new drug development; International Drug Discovery Science and Technology 2010; 2010 Oct 24; Beijing, China.

V. NATIONAL PROFESSIONAL RECOGNITION

June E. Ayling: Reviewer, American Journal of Clinical Nutrition, Photochemistry and Photobiology, PLoS ONE, and Journal of Nutrition.

Natalie Bauer: Member, American Thoracic Society Programming Committee; Gilead Sciences Research Scholars Program, Pulmonary Arterial Hypertension; American Thoracic Society Thematic Poster Session Facilitator; Reviewer, American Journal of Physiology: Lung Cell and Molecular Biology; Physiological Reviews; Study Section Member, American Lung Association and American Heart Association; and Nominating Committee Member, Gulf Coast Physiological Society.

Eugene A. Cioffi: Reviewer and Co-Editor, Current Topics in Medicinal Chemistry; Reviewer, Journal of Physical Chemistry, Journal of Organic Chemistry, Synthesis, Synthetic Communications, Bioorganic & Medicinal Chemistry, Carbohydrate Research, Journal of Labeled Compounds and Radiopharmaceuticals, Environmental Science and Technology; Grant reviewer, National Science Foundation and National Institutes of Health.

Mark N. Gillespie: Facilitator for several sessions of the American Thoracic Society International Conference, 2011 May 17, Denver, CO. Received the Outstanding Graduate Alumni Award for the University of Kentucky Ph.D. program in Pharmaceutical Sciences. Honored at the Symposium on Drug Discovery and Development at the University of Kentucky in Lexington on Oct 15, 2010. Outgoing chair, Pulmonary Circulation Assembly, American Thoracic Society.

Ivan F. McMurtry: Editor (along with M. Gillespie, T. Stevens, and W. Wagner), American Physiology Society's new online journal, Comprehensive Physiology: Topic on Pulmonary Circulation and Non-Respiratory Functions; International Associated Editor, Circulation Journal; Reviewer, American Journal of Physiology Lung Cell Mol Physiology (Star Reviewer), American Journal of Physiology Heart and Circulation, American Journal of Respiratory Critical Care Medicine, American Journal Respiratory Cellular Molecular Biology, European Respiratory Journal, Cardiovascular Research, Circulation Journal, Journal of Applied Physiology, Journal of Vascular Research, Physiology Review, and Nature Medicine. Participated in Clinical Trials Review Committee, NHLBI, review of grant applications by Ronald Oudiz and Andrzei Stansilaw Kosinsiki.

<u>Thomas C. Rich</u>: Reviewer, American Heart Association Signaling II Peer Review Study Group; Ad hoc reviewer, *Nature Protocols*, *American Journal of Physiology – Cell*; *American Journal of Physiology – Lung*; and *Cardiovascular Pharmacology*.

Stephen W. Schaffer: Editorial Board, Molecular Cellular Biochemistry; Secretary, International Academy of Cardiovascular Sciences, Cardiac Bio BcT2 study section,

American Heart Association Apr and Oct 2011; organizer for 12th International Congress on Amino Acids, Peptides and Proteins, Beijing, China; Editor, Vascular Pharmacology on Mechanisms of Vascular Dysfunction in Diabetes.

<u>Troy Stevens</u>: Awarded a Method to Extend Research in Time (MERIT) award by the National Institutes of Health. This award could extend his research funding from the NIH's National Heart, Blood and Lung Institute through 2021. Associate editor: AJP-Lung; Program Project Grant Reviewer: National Institutes of Health; Program Project Grant External Advisor: Medical College of Georgia and University of Pennsylvania; SEPt Grant Reviewer: National Institutes of Health.

Wiltz W. Wagner, Jr.: Facilitator, several sessions during American Thoracic Society International Conference; 2011 May 13-18; Denver, CO.

VI. BRIEF SUMMARY OF ACTIVITIES AND PROGRESS

The Department of Pharmacology hosted visits from several scientists who participated in the Distinguished Scientist Seminar Series: Dr. Michael Jay, Fred N. Eshelman Distinguished Professor, Division of Molecular Pharmaceutics, Nanotechnology in Drug Delivery, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, presented a seminar entitled "Commercialization of University-Based Research: One Professor's Sojourn" on Thursday, October 7, 2010. Dr. Nicholas S. Hill, Professor of Medicine Tufts University School of Medicine, Chief, Pulmonary and Critical Care and Sleep Division, Tufts Medical Center, Boston MA, presented a seminar entitled "Serotonin Signaling in Pulmonary Hypertension" on December 16. 2010. Dr. Alan G. Marshall, Robert O. Lawton Professor of Chemistry and Biochemistry. Director, Ion Cyclotron Resonance Program, National High Magnetic Field Laboratory. Florida State University, Tallahassee, FL, presented a seminar entitled "Accurate Mass Measurement: Taking Full Analytical Advantage of Nature's Isotopic Complexity" on February 17, 2011. Dr. Marie Celeste Simon, Scientific Director and Investigator, Abramson Family Cancer Research Institute, Investigator, Howard Hughes Medical Institute, Professor and Investigator, University of Pennsylvania, School of Medicine, Department of Cell and Developmental Biology/AFCRI Philadelphia, PA, presented a seminar entitled "HIFs, Hypoxia, and Tumor Progression" on April 21, 2011.

Five students graduated from the Department of Pharmacology. Dr. Audrey A. Vasauskas' defense was on October 5, 2010. Her dissertation was entitled "Expression and Storage of Squirrel Monkey Chorionic Gonadotropin in the Pituitary Gland." Dr. Vasauskas is a Post-Doctoral Fellow in Dr. Donna Cioffi's lab in the Department of Biochemistry. Dr. Jonathan Scammell was her major professor. Dr. Darla J. Reed's defense was on October 28, 2010. Her dissertation was entitled "Nuclear Oxidant Stress in Hypoxia." Dr. Abu-Bakr Al-Mehdi served as her major professor. Dr. Christina Barry McManus' defense was on March 18, 2011. Her dissertation was entitled "Calcium Entry Through the Store-Operated Calcium Current, *Isoc*, Disrupts the Spectrin-F-Actin Interaction Inducing Inter-Endothelial Gaps." Dr. Troy Stevens served as her major professor. Dr. Barry-McManus is working with the American Red Cross in Birmingham,

AL. Dr. Glenda-Para-Bonilla's defense was on May 9, 2011. Her dissertation was entitled "Essential Role of Lactate Dehydrogenase-A (LDH-A) in the Proliferative and Neo-angiogenic Phenotype of Pulmonary Microvascular Endothelial Cells." Dr. Troy Stevens was her major professor. Dr. Wei P. Feinstein's defense was on June 10, 2011. Her dissertation was entitled "Quantitative Assessment of Cellular Mechanisms Contributing to the Localization of cAMP signals." Dr. Thomas Rich was her major professor. Dr. Salina Gairhe graduated in May 2011. Her dissertation was entitled "Myoendothelial Gap Junctional Signaling Regulates Pulmonary Arterial Smooth Muscle Phenotype." Dr. Ivan McMurtry was her major professor. Dr. Gairhe is a Post-Doctoral Fellow in the USA Department of Pharmacology.