

1999-2000
SUMMARY OF SCHOLARLY ACTIVITIES
DEPARTMENT OF PHARMACOLOGY

I. ARTICLES PUBLISHED IN BOOKS AND JOURNALS

A. Full length published articles.

J.E. Ayling, S.W. Bailey, S.R. Boerth, R. Giugliani, C. Braegger, B. Thöny and N. Blau. Hyperphenylalaninemia and 7-Pterin Excretion Associated With Mutations in 4a-Hydroxy-Tetrahydrobiopterin Dehydratase/DCoH: Analysis of Enzyme Activity in Intestinal Biopsies. *Mol. Gen. Metab.* 70: 179-188 (2000).

P. Babal, S.M. Manuel, J.W. Olson, and M.N. Gillespie. Regulation of Polyamine Uptake by Hypoxia in Rat Lungs and Pulmonary Arteries. Interactions Between Endothelial and Smooth Muscle Cells. *Am. J. Physiol. Lung Cell Mol. Physiol.* 278:L610-L617 (2000).

S.W. Bailey and J.E. Ayling. Food and Vitamin Preparations Containing the Natural Isomer of Reduced Folates. Australian Patent #722050 (2000).

D.M. Baldisseri, R.R. Rustandi, Z. Zhang, C. Tang, C.L. Blair, A. Landar, D.B. Zimmer, and D.J. Weber. ^1H , ^{13}C , ^{15}N NMR Sequence-Specific Resonance Assignments for Rat Apo-S100A1($\alpha\alpha$). *J. Biomol. NMR* 14:91-92 (1999).

V. Grishko, N.N. Druzhyna, S.P. LeDoux, and G.L. Wilson. Nitric Oxide-Induced Damage to mtDNA and Its Subsequent Repair. *Nucl. Acids Res.* 27(22):4510-4516 (1999).

W. Hoffman, D. Schubert, J. LaBonte, L. Munson, S. Gibson, J.G. Scammell, P. Ferrigno, and J. Sodroski. Species-Specific, Postentry Barriers to Primate Immunodeficiency Virus Infection. *J. Virol.* 73:10020-10028 (1999).

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M.S. Mozaffari, C. Patel, B. Warren, and S.W. Schaffer. NaCl-Induced Hypertensive Rat Model of Noninsulin-Dependent Diabetes: Role of Sympathetic Modulation. *Am. J. Hypertens.* 13:540-546 (2000).

A. Ramsey, L.C. Russell, S.R. Whitt, and M. Chinkers. Overlapping Sites of Tetratricopeptide Repeat Protein Binding and Chaperone Activity in Heat Shock Protein 90. *J. Biol. Chem.* 275:17857-17862 (2000).

J.G. Scammell. Steroid Resistance in the Squirrel Monkey: An Old Subject Revisited. *ILAR J.* 41:19-25 (2000).

J.G. Scammell, S. Reddy, D.L. Valentine, T.N. Coker, S.N. Nikolopoulos, and R.A. Ross. Isolation and Characterization of the Human Secretogranin II Gene Promoter. *Mol. Brain Res.* 75:8-15 (2000).

S.W. Schaffer, C. Ballard-Croft, and V. Solodushko. Cardioprotective Effects of Chronic Hyperglycemia: Effect of Hypoxia-Induced Apoptosis and Necrosis. *Am. J. Physiol.* 278:H1948-H1954 (2000).

S.W. Schaffer, J.B. Lombardini, and J. Azuma. Interaction between the Actions of Taurine and Angiotensin II. *Amino Acids* 18:305-318 (2000).

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S. Wu, A. Bhattacharjee, M. Zhang, L. Liu, and M. Li. A Metabolite of Mebfradil Inhibits L-Type Calcium Currents in the Pancreatic β -Cells. *J. Pharm. Exp. Ther.* 292:939-943 (2000).

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B. Articles in press.

M. Azuma, K. Takahashi, T. Fukuda, Y. Ohyabu, I. Yamamoto, S. Kim, H. Iwao, S.W. Schaffer, and J. Azuma. Taurine Attenuates Hypertrophy Induced by Angiotensin II in Primary Cultured Neonatal Rat Cardiac Myocytes. *Eur. J. Pharmacol.* (2000).

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S.W. Schaffer, K. Takahashi, and J. Azuma. Role of Osmoregulation in the Actions of Taurine. *Amino Acids* (2000).

T. Stevens, J.G.N. Garcia, D.M. Shasby, J. Bhattacharya, and A.B. Malik. Mechanisms Regulating Endothelial Cell Barrier Function. *Am. J. Physiol.* (2000).

W.J. Thompson, T. Ashikaga, J.J. Kelly, Li Liu, B. Zhu, L. Vemavarapu, and S.J. Strada. Regulation of cAMP in Rat Pulmonary Microvascular Endothelial Cells by Rolipram-Sensitive cAMP Phosphodiesterase (PDE4). *Biochem. Pharmacol.* (2000).

D. Weber, R. Rustandi, and D.B. Zimmer. Interaction of Dimeric S100B(β) With the Tumor Suppressor Protein p53: A Model for Ca^{2+} -Dependent S100 Target Protein Interactions. IN: R. Pochet (Ed.) CALCIUM: The Molecular Basis of Calcium Action in Biology and Medicine. Kluwer Academic Publishers, Netherlands (2000).

D.B. Zimmer and D.W. Weber. Structure and Function of S100 Proteins. *Cell Biochem. Biophys.* (2000).

II. PUBLISHED ABSTRACTS.

S.W. Bailey, M.R. Malinow, and J.E. Ayling. An HPLC Method for Analysis of Unreduced Folic Acid in Blood. *FASEB J.* 14:LB204 (2000).

K. Bonness, I. Durcova, G. Capley, T. Stevens, M.N. Gillespie, and J.W. Olson. Thrombin Stimulates Sub-Cellular Trafficking of Active Ornithine Decarboxylase in Rat Pulmonary Endothelial Cells. *FASEB J.* 14:A692 (2000).

J.F. Breit, K.A. Ziel, P. Babal, J.W. Olson, and M.N. Gillespie. Potential Role for the Protease-Activated Receptor-2 (PAR-2) in Hypoxia-Induced Polyamine Transport in Pulmonary Artery Smooth Muscle Cells (PASMCs). *FASEB J.* 14: A126 (2000).

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C.C. Campbell, M. Ruchko, P. Babal, G.C. Capley, S.K. Gilmour, J.W. Olson, and M.N. Gillespie. Agmatine (AGM)-Mediated Effects on Pulmonary Artery Endothelial Cell Polyamine Regulatory Pathways: Role of Antizyme. *FASEB J.* 14: A409, 2000.

G. Capley, M. Ruchko, Y. Zhang, M.N. Gillespie, and J.W. Olson. Monocrotaline Pyrrole-Induced Nuclear Translocation of β -Catenin and the Regulation of c-MYC Transcription in Rat Pulmonary Endothelial Cells. *FASEB J.* 14:A692 (2000).

L. Chen, P.H. Roberts, E.J. Meehan, K.L. Gross, S.W. Bailey, and J.E. Ayling. Crystal Structure of 4a-OH-Tetrahydropterin Dehydratase/DCoH Complexed With a Substrate Analog. Am. Crystallographic Assn. W0133 (2000).

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V. Grishko, M. Solomon, S.P. LeDoux, G.L. Wilson, and M.N. Gillespie. Xanthine Oxidase-Induced Mitochondrial DNA Damage in Pulmonary Vascular Endothelial Cells Mapped at Nucleotide Resolution. Free Radic. Biol. Med. 27(1):S105 (1999).

J. Haynes, B. Obiako, P. Babal, G. Brough, and T. Stevens. 5'-(N-Ethylcarboxamido) Adenosine Rapidly Desensitizes the A₂ Adenosine Receptor in Lung Circulation. Am. J. Resp. Crit. Care Med. 159:A574 (1999).

R.E. Honkanen, G. Urban, J.G. Scammell, and N.M. Dean. Negative Regulation of Glucocorticoid Receptor-Mediated Growth Arrest by Ser/Thr Protein Phosphatase Type 5 (PP5). Proc. Am. Assn. Cancer Res. 41:27 (2000).

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C. Tang, F. Carrier, D.B. Zimmer, and D.J. Weber. Abrogation of p53-Dependent Transcription Activation by S100 Calcium-Binding Proteins. *11th Int. Symp., Calcium-Binding Proteins and Calcium Function in Health and Disease, Kisarazu, Japan*, pp. III-2 (1999).

S. Wu, G. Brough, J. Creighton, M. El-Menshawi, S. Goodman, and T. Stevens. Disruption of F-actin Binding to Non-Erythroid Spectrin Induces Focal Inter-Endothelial Cell Gaps. *FASEB J.* 14:A694 (2000).

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M. Zhang and M. Li. T-type Calcium Currents Are Involved in Rat Islet β -cell Proliferation. *FASEB J.* 14(4):A110 (2000).

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K.A. Ziel, J.F. Breit, P. Babal, J.W. Olson, and M.N. Gillespie. An Endothelial Cell-Derived, Trypsin-Like Protease Enables Hypoxic Induction of Main Pulmonary Artery Smooth Muscle Polyamine Transport. *FASEB J.* 14: A126, (2000).

D.B. Zimmer and J. Chaplin. Organization, Expression and Evolution of the S100A1 Gene Locus. 11th Int. Symp., Calcium-Binding Proteins and Calcium Function in Health and Disease, Kisarazu, Japan, p. III-1 (1999).

III. BOOKS PUBLISHED

None.

IV. PRESENTATIONS

J.E. Ayling. Hyperphenylalaninemia Associated With Mutations in 4a-Hydroxy-Tetrahydropterin Dehydratase/DChH: Analysis in Intestinal Biopsies. 12th Int. Conf. Pteridines and Related Biogenic Amines, St. Moritz, Switzerland (2000).

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J. Scammell. Squirrel Monkey FKBP51 Is a Potent Inhibitor of Glucocorticoid Receptor Binding. Immunophilins: Cellular Functions and Immunosuppressive Drug Targets, Keystone Symp., Keystone, CO (2000).

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T. Stevens. Control of Endothelial Cell Barrier Function by Calcium and cAMP. Dept., Pharmacol., Univ. of Illinois, Chicago, IL (2000).

T. Stevens. Calcium Regulation of cAMP: Control of Endothelial Permeability. Exp. Biol. Mtg., San Diego, CA (2000).

T. Stevens. Signal Transduction in Control of Macro- and Microvascular Endothelial Cell Function. NIH, Bethesda, MD (2000).

D.B. Zimmer. Organization, Expression and Evolution of the S100A1 Gene Locus. 11th Int. Symp., Calcium-Binding Proteins and Calcium Function in Health and Disease, Kisarazu, Japan (1999).

V. NATIONAL PROFESSIONAL RECOGNITION

The Department of Pharmacology had three faculty members who served on editorial boards of major journals. Dr. Mark Gillespie served on the Editorial Board of the *American J. of Physiology*, Dr. Stephen Schaffer on *Molecular and Cellular Biochemistry*, Section Editor for *Amino Acids*; and Dr. Samuel Strada on *CNS Drug Reviews*. Dr. Jonathan Scammell was appointed to the Editorial Advisory Board of *Journal of Pharmacology and Experimental Therapeutics*.

A number of faculty members served on various committees for national and international conferences, review boards, and study sections. Dr. June Ayling served on the International Scientific Committee for the 12th International Conference on Pterins, Folates and Related Biogenic Amines. Dr. Mark Gillespie served on the Lung Biology and Pathology Study Section, Special Study Section on Biological Effects of Intermittent Hypoxia, and Special Study Section on STTR/SBIR grants for NIH; served on the Long Range Planning Committee; and Chaired the Nominating Committee of the American Thoracic Society; Dr. Jack Olson served as Merit Reviewer for the Department of Veteran Affairs. Dr. Jonathan Scammell is a member of the Biochemical Endocrinology Study Section, NIH. Dr. Stephen Schaffer served on the Review Board

of the Southern Consortium, American Heart Association, and Ad-Hoc member of NSBRI Study Section. Dr. Troy Stevens served as an Ad Hoc Member of the Lung Biology and Pathology Study Section, NHLBI, and the Applied Physiology Study Section, RAP; Chaired symposium on the Mechanisms Regulating Endothelial Cell Permeability for Experimental Biology; Chaired NIH Workshop on Endothelial Cell Phenotypes; and served on the Pulmonary Circulation Planning and Program Committees for the American Thoracic Society. Dr. Samuel Strada was appointed to the Nominating Committee Council of Academic Societies, AAMC; served as Representative for the Association for Medical School Pharmacology; and participated in a site visit to evaluate the Department of Pharmacology at Loyola University.

The Department received additional funding through a number of research grant awards. Dr. Jack Olson received a Grant-in-Aid from the American Heart Association, Southern Consortium for research on "Pulmonary Endothelial Cell Wound Repair and Polyamines". Dr. Danna Zimmer received two subcontract grants, one with Boston University from NIH entitled "Deciphering the Cellular Functions of Aldolase," and another with the University of Maryland from the American Cancer Society entitled "Studies on Interactions between p53 and S100 Proteins."

Patents of Dr. Steven Bailey and Dr. June Ayling have resulted in a licensing agreement with Merck KGaA, Darmstadt, Germany, to market world-wide "Food and Vitamin Preparations Containing Natural Reduced Folates." If Merck is successful in marketing the product, the royalties generated could provide a substantial source of income for the College of Medicine.

VI. BRIEF SUMMARY OF DEPARTMENTAL ACTIVITIES AND PROGRESS

Dr. Arin Bhattacharjee and Dr. David Killilea completed the requirements for the Ph.D. degree in Basic Medical Sciences. Dr. Bhattacharjee conducted his research in the laboratory of Dr. Ming Li. His dissertation was entitled "Functional Characterization of T-Type Ca^{2+} Channels in Pancreatic β -Cells." Dr. Killilea conducted his research in the laboratory of Dr. Mark Gillespie. His dissertation was entitled "Oxidative Stress in Hypoxic Signal Transduction."

Ms. Natalie Norwood was awarded the 2000 Proctor & Gamble Professional Opportunity Award for Meritorious Research by the Council of the American Physiological Society. Ms. Norwood was one of seventeen recipients selected by the Steering Committee of the Respiration Section. Her presentation was entitled "Distinct Regulation of Endothelial Cell Permeability by Proteolytic and Direct Activation of the Thrombin Receptor."

The Department hosted visits by several distinguished scientists: Drs. Piero Anversa (New York Med. Col.), Bruce Freeman (Univ. of Alabama, Birmingham), Richard Gaber (Northwestern Univ.), William Parks (Washington Univ.), and Marlene Rabinovitch (Univ. of Toronto).