

1999-2000
SUMMARY OF SCHOLARLY ACTIVITIES
DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR BIOLOGY

I. ARTICLES PUBLISHED IN BOOKS AND JOURNALS.

A. Full-length published articles.

N.N. Aronson, Jr. Aspartylglycosaminuria: Biochemistry and Molecular Biology. *Biochim. Biophys. Acta: Molecular Basis for Disease* 8;1455(2-3):139-54 (1999).

N.N. Aronson, Jr. (1) Lysosomal Degradation of Glycoproteins, pp. 473-494; and (2) Lysosomal Storage Diseases, pp. 946-958. IN: B. Ernst, G. Hart, and P. Sinay (Eds.) *Oligosaccharides in Chemistry and Biology: A Comparison Handbook*. Wiley-VCH, Weinheim, Germany (2000).

V. Bracchi-Ricard, S. Barik, C. Delvecchio, C. Doerig, R. Chakrabarti, and D. Chakrabarti. PfPK6, a Novel Cyclin-Dependent Kinase/Mitogen-Activated Protein Kinase-Related Protein Kinase From *Plasmodium Falciparum*. *Biochem. J.* 347:255-263 (2000).

E. Burke, N.M. Mahoney, S.C. Almo, and S. Barik. Profilin Is Required for Optimal Actin-Dependent Transcription of Respiratory Syncytial Virus Genome RNA. *J. Virol.* 74(2):669-675 (2000).

X. Chen, T. Ansai, S. Awano, T. Iida, S. Barik, and T. Takehara. Isolation, Cloning, and Expression of an Acid Phosphatase Containing Phosphotyrosyl Phosphatase Activity From *Prevotella intermedia*. *J. Bacteriol.* 22:7107-114 (2000).

A. Cheng, N. Dean, and R.E. Honkanen. Serine/Threonine Protein Phosphatase Type 1 γ 1 (PP1 γ 1) Is Required for the Completion of Cytokinesis in Human A549 Lung Carcinoma Cells. *J. Biol. Chem.* 275(3):1846-1854 (2000).

J.H. Connor, T. Kleeman, S. Barik, R.E. Honkanen, and S. Shenolikar. Importance of the β 12 - β 13 Loop in Protein Phosphatase-1 Catalytic Subunit for Inhibition by Toxins and Mammalian Protein Inhibitors. *J. Biol. Chem.* 274(32):22366-22372 (1999).

L.C. Dupuy, S. Dobson, V. Bitko, and S. Barik. Casein Kinase 2-Mediated Phosphorylation of Respiratory Syncytial Virus Phosphoprotein P Is Essential for the Transcription Elongation Activity of the Viral Polymerase; Phosphorylation by Casein Kinase 1 Occurs Mainly at Ser(215) and Is Without Effect. *J. Virol.* 73(10):8384-8392 (1999).

J.W. Gaubatz. Base Modification in Aging. IN: B.A. Gilchrest and W. Bohr (Eds.) The Role of DNA Damage and Repair in Cell Aging, Elsevier Science, Amsterdam, pp. 41-72 (2000).

R.E. Honkanen and N. Dean. Antisense Oligonucleotide Modulation of Human Serine/Threonine Protein Phosphatase Gene Expression. Serial Number 08/951,211; Patent Number 5,948,902 (1999).

X. Huang, M.R. Swingle, and R.E. Honkanen. Photoreceptors Serine/Threonine Protein Phosphatase Type 7 (PP7): Cloning, Expression and Functional Analysis. *Methods Enzymol.* 315:579-593 (2000).

M.G. Nair. Antifolate Drugs in Cancer Therapy. *Drug Discovery Today* 4:492-494 (1999).

M.G. Nair. Three New Non-Polyglutamylatable, Folates and Process for Preparing the Same. Letters Patent. Japan. 2,958,902 (1999).

A. Sjöholm and R.E. Honkanen. Polyamines Regulate Serine/Threonine Protein Phosphatases in Insulin-Secreting Cells. *Pancreas* 20(1):32-37 (2000).

B. Articles in Press

N.N. Aronson, Jr. Glycosylasparaginase: Molecular Medicine. IN: T. E. Creighton (Ed) The Encyclopedia of Molecular Medicine. John Wiley & Sons, New York, NY (2000).

V. Bitko and S. Barik. An Endoplasmic Reticulum-Specific Stress-Activated Caspase (Caspase-12) Is Implicated in the Apoptosis of A549 Epithelial Cells by Respiratory Syncytial Virus. *J. Cell. Biochem.* (2000).

J.H. Heidecker, U.K. Nair, and J.D. Funkhouser. An ANF-3 Binding Element in the APN Promoter Is Required for High-Level Lung Expression. *Excerpta Medica International Congress Series* (2000).

R.E. Honkanen. Serine/Threonine Protein Phosphatases. IN: Stanley T. Crooke (Ed.) Antisense Drug Technology: Principles, Strategies and Applications (2000).

R.E. Honkanen. Decreasing Cell Proliferation by Decreasing Levels of PP5. Serial Number 08/975,127. Patent Pending (1999).

R.E. Honkanen. Glucocorticoid Receptor Agonist and Decreased PP5 Expression. Serial Number 09/282,736. Patent Pending (1999).

M.G. Nair, M. Fayard, A. Amato, J. Lariccia, J. Mallett, S. Miles, and R.L. Kisliuk. Metabolism-Based Drug Design. Proc., Frontiers in Pharmacol. Ther. (2000).

II. PUBLISHED ABSTRACTS

S. Dobson, D. Chakrabarti, V. Bracchi, and S. Barik. Cloning and Expression of a Novel Phosphatase (PPJ) in *Plasmodium Falciparum*. FASEB Summer Res. Conf.; Protein Phosphatases, p. 11 (2000).

J.G. Dubuisson, R. Southard, D.L. Dyess, and J.W. Gaubatz. Resveratrol Inhibits Phase II Activation of the Food Mutagen H-Hydroxy-PhIP by Human Mammary Epithelial Cells and Enzymes. 9th Annu. Res. Conf., Am. Institute for Cancer Res., p. 18 (1999).

J.D. Funkhouser, J.R. Heidecker, and U.K. Nair. A HNG-3 β Binding Element in the Aminopeptidase N/CD13 Gene Promoter Is Required for High-Level Expression in Lung Epithelial Cells. Int. Conf., Cell Surface Aminopeptidases, p. 65 (2000).

J.W. Gaubatz, J.G. Dubuisson, R. Southard, and D.L. Dyess. Nutrient Modulation of Heterocyclic Amine Phase II Mutagen Activation Enzymes: Human Mammary Epithelial Cells. ASBMB Fall Symposia: Nutrient Control of Gene Transcription, p. 8 (1999).

J.W. Gaubatz, J. Dubuisson, R. Southard, W. Murph, Jr., A. Shaw, and D.L. Dyess. Kinase Phase II Activation of Mutagens by Human Mammary Epithelial Cells. FASEB J. 14:A525 (2000).

J.W. Gaubatz, W. Murph, Jr., and J. Dubuisson. Metabolic Activation Pathways for Heterocyclic Amine Mutagens in Cardiac Myocytes. FASEB J. 14:A525 (2000).

T. A. Golden, I. Aragon, G. Urban, S.R. Cooper, L.M. Watts, N.M. Dean, and R.E. Honkanen. Development of Antisense Oligonucleotides that Specifically Inhibit the Expression of Serine/Threonine Protein Phosphatase Type 5 (pp5) *in vivo*. FASEB Summer Res. Conf.; Protein Phosphatases, p. 12 (2000).

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: p. 27 (2000).

M.G. Nair. Metabolism-Based Antifolate Drug Design. Proc., Int. Cong. Pharmacol. 21st Century, p. 40 (1999).

M.R. Swingle and R.E. Honkanen. Pharmacological Characterization of Bovine Serine/Threonine Protein Phosphatase Type 5 (PP5). FASEB Summer Res. Conf.; Protein Phosphatases, p. 15 (2000).

G. Urban, D.A. Dean, M.S. Swingle, N.M. Dean, and R.E. Honkanen. Serine Threonine Protein Phosphatase 5 (pp5) Regulates the Nucleocytoplasmic Trafficking of the Glucocorticoid Receptor Complex. FASEB Summer Res. Conf.; Protein Phosphatases, p. 16 (2000).

III. BOOKS PUBLISHED

None.

IV. PRESENTATIONS

S. Barik. Functional Genomics of Host-Virus Interaction. Antiviral Res. Div., Wyeth-Ayerst Research, Pearl River, NY (2000).

J.W. Gaubatz. Nutrient Modulation of Heterocyclic Amine Phase II Mutagen Activation Enzymes: Human Mammary Epithelial Cells. ASBMB Fall Symposia: Nutrient Control of Gene Transcription, Taos, NM (1999).

J.W. Gaubatz. Resveratrol Inhibits Phase II Activation of the Food Mutagen N-Hydroxyl-PhIP by Human Mammary Epithelial Cells and Enzymes. AICR, Nutrition and Cancer Prevention, Washington, DC (1999).

J.W. Gaubatz. Kinase Phase II Activation of Mutagens by Human Mammary Epithelial Cells. Gordon Res. Conf.: Mammary Gland Biol., Lucca, Italy (2000).

J.W. Gaubatz. Metabolic Activation Pathways for Heterocyclic Amine Mutagens. ASBMB Annu. Mtg., Boston, MA (2000).

R.E. Honkanen. Serine/Threonine Protein Phosphatases and the Regulation of Cell Proliferation: PP5 an Emerging Key Regulator of Growth. Department of Biological Sciences, Florida State University, Tallahassee, FL (2000).

R. E. Honkanen. Negative Regulation of Glucocorticoid Receptor-Mediated Growth Arrest by Ser/Thr Protein Phosphatase Type 5 (PP5). Am. Assn. Cancer Res., San Francisco, CA (2000).

R.E. Honkanen. Serine/Threonine Protein Phosphatases and the Regulation of Cellular Signaling: PP5 an Emerging Key Regulator of Both p53 and Glucocorticoid Mediated Growth Arrest. Division of Pulmonary and Critical Care Medicine, Northwestern University, Chicago, IL (2000).

R.E. Honkanen. Serine/Threonine Protein Phosphatase Type 5, an Emerging Star in the Regulation of Cellular Proliferation. Rigel Pharmaceuticals, San Francisco, CA (1999).

R.E. Honkanen. Protein Phosphatase Type 5, a Key Regulator of Cellular Proliferation. Department of Pharmacology, East Tennessee State University, Johnson City, TN (1999).

R.E. Honkanen. Ser/Thr Protein Phosphatase Type 5(PP5) Functions as a Negative Regulator of Glucocorticoid Receptor-Mediated Growth Arrest. EMBO Workshop, Euro Phosphatase 99, Leuven , Belgium (1999).

R.E. Honkanen. Protein Phosphatase Type 5 (PP5), a Regulator of Hormone-Mediated Growth. FASEB Summer Res. Conf.: Protein Phosphatases, Copper Mountain, CO (2000).

V. NATIONAL PROFESSIONAL RECOGNITION.

Biochemistry faculty participated on a number of national committees this past year. Dr. S. Barik was a reviewer for several journals: *BioTechniques*, *Journal of Virology*, and *Biochemical Pharmacology*. Dr. Barik also was a candidate for Vice President for the Southeastern Society for Parasitologists; Dr. Jane Funkhouser served on the Editorial Board of the *American Journal of Physiology, Lung Cellular & Molecular Physiology* and served as a reviewer for the NIH Lung Biology & Pathology Study Section; Dr. James Gaubatz reviewed grants for the National Institutes of Health, Nutrition Study Section, and was a Member of the National Scientific Advisory Council of the American Federation for Aging Research. Dr. Aronson is a member of the Board of Directors of the Association of Medical and Graduate Departments of Biochemistry.

VI. BRIEF SUMMARY OF DEPARTMENT ACTIVITIES AND PROGRESS.

Biochemistry Graduate students achieved excellent progress in the 1999-2000 academic year. Two students attended the FASEB Protein Phosphatase Copper Mountain, Colorado, Conference to present their research: Sean Dobson (S. Barik's laboratory) made a poster presentation: "Cloning and Expression of a Novel Phosphatase (PPJ) in *Plasmodium falciparum*"; and Mark Swingle (R. Honkanen's laboratory) described his work on: "The Pharmacological Characterization of Bovine Serine/Threonine Protein Phosphatase 5." John Rodriguez (R. Honkanen's laboratory) was awarded a 5-year NIH predoctoral fellowship. Brian Adams, who graduated from the USA Biomedical Sciences program, is our only new biochemistry Ph.D. graduate student for Fall 2000.

Three medical students completed summer research projects in Biochemistry. Alicia Logue, a first-year student, made an oral presentation: "Investigation of Ectopeptidase Expression in Epithelial Cell Lines," based on work with Dr. J. Funkhouser; Beth Miller, a second year student, spoke on: "Characterization of Serine/Threonine Protein Phosphatases Associated with Fostriecin Mediated Protection to Ischemic Cardiac Tissue," from studies done with Dr. R. Honkanen; and Naghma Khan, an MD-Ph.D. student, had a poster presentation: "Identification of Genes of Human Lung Epithelial Cells Regulated by Respiratory Syncytial Virus Infection," based on her summer project with Dr. S. Barik. Naghma Khan won the best poster presentation award for the Summer Research Program.

The Biochemistry Department spent a significant effort trying to recruit a new faculty member in the area of cancer research. Currently, the position remains open. A number of Biochemistry faculty are involved in patents and other aspects of university/industry collaborations. Dr. Honkanen continues work with ISIS Pharmaceuticals in Carlsbad, California on antisense RNA drugs directed at regulating protein phosphatases. In addition, the College of Medicine and Rigel Pharmaceuticals in San Francisco culminated a licensing agreement related to one of Dr. Honkanen's patents on medical applications for protein phosphatases. Educational efforts and accomplishments of the Biochemistry faculty were recognized by the College of Medicine graduating class of 2000. Over 50% of the faculty members, Drs. Aronson, Barik, Funkhouser, and Lane, were honored for excellence in teaching at the Senior Honors Convocation.