

The Institute of Maternal-Fetal Biology

A Research Institute of the University of Kansas
Healthy Mothers, Healthy Babies



Annual Report

September 2002-February 2004

The Institute of Maternal-Fetal Biology

Our Mission: *To improve the quality of life of mothers and babies.*

Members of the Institute perform basic life sciences research and participate in the training of future scientists.

Our Research

Institute scientists investigate genes and proteins and their involvement in regulating maternal adaptations to pregnancy, placental biology and fetal development.

Currently, research focuses on:

Diseases of Pregnancy

- * Preeclampsia
- * Early Pregnancy Loss
- * Intrauterine Growth Restriction
- * Immunology of Pregnancy

Diseases of the Fetus

- * Those Associated with Blood Cell Formation (anemias, thalassemias)
- * Sexual Development
- * Maternal Substance Abuse
- * Those Leading to Birth Defects
- * Pulmonary Development & Mechanisms of Lung Injury

The fundamental knowledge derived from these research efforts will permit the rational design of therapeutics to promote the health of mothers and babies.

IMFB
Sponsored Seminars
(September 2002-February 2004)

“Redefining Self: Long-term Persistence of Maternal and Fetal Cells”, J. Lee Nelson, M.D., Fred Hutchinson Cancer Research Center, Division of Rheumatology

“The Placenta and IGF-I: Pivotal Roles in the Coordination of Human Fetoplacental Growth?” Nicholas Illsley, Depts. of Obstetrics and Gynecology and Women’s Health, Pharmacology and Physiology, New Jersey Medical School

“How does the mother cure a placental infection without aborting the fetus?” Jeffrey W. Pollard, Dept. of Developmental Biology and Cancer, Albert Einstein College of Medicine

“BMPs and Early Lineage Decisions of Human Embryonic Stem Cells”, Ren-He Xu, M.D., Ph.D., WiCell Research Institute, University of Wisconsin Medical School

“A causative relationship exists between eosinophils and the development of allergic pulmonary pathologies in the mouse”, James J. Lee, Ph.D., Dept. of Biochemistry and Molecular Biology, Mayo Clinic – Scottsdale, AZ

“Developmental biology and functional role of uterine endometrial glands”, Thomas E. Spencer, Ph.D., Center for Animal Biotechnology and Genomics, Texas A & M University

“Chemical Mutagenesis in Mouse Embryonic Stem Cells: Development of Genetic Tools to Study TGF-beta Signaling”, Jay L. Vivian, Ph.D., Dept. of Genetics, University of North Carolina-Chapel Hill

“The Battle of the Sexes: Controlling the Fate of the Mammalian Gonad”, Blanche Capel, Ph.D., Dept. of Cell Biology, Duke University

IMFB RESEARCHERS

The current research group consists of ten laboratories directed by faculty from the University of Kansas School of Medicine in Kansas City, Kansas, The University of Kansas School of Pharmacy in Lawrence, Kansas, and Children's Mercy Hospitals and Clinics in Kansas City, Missouri.



Glen K. Andrews, Ph.D.
Professor
Biochemistry & Molecular
Biology, Univ. of Kansas
School of Medicine.



Kenneth R. Peterson, Ph.D.
Associate Professor
Biochemistry & Molecular
Biology, Univ. of Kansas
School of Medicine. *Gene
regulation in developing
red blood cells.*



Kenneth L. Audus, Ph.D.
Professor and Chair,
Pharmaceutical Chemistry,
Univ. of Kansas School of
Pharmacy. *Drug transport
across the placental barrier.*



Margaret G. Petroff, Ph.D.
Research Assistant Professor
Anatomy and Cell Biology
Univ. of Kansas School of
Medicine. *Immunology of
placental cells.*



Alan R. Godwin, Ph.D.
Assistant Professor
Molecular & Integrative
Physiology, Univ. of Kansas
School of Medicine. *Genetic
control of morphogenesis.*



Michael J. Soares, Ph.D.
Director, Institute of Maternal-
Fetal Biology, Professor,
Molecular & Integrative
Physiology, Univ. of Kansas
School of Medicine.
*Molecular endocrinology of
pregnancy.*



Leslie L. Heckert, Ph.D.
Assistant Professor and
Self-Scholar, Molecular &
Integrative Physiology
Univ. of Kansas School of
Medicine. *Gene regulation
in the developing
reproductive system.*



William E. Truog, M.D.
Sosland Family Professor
of Pediatrics, Children's Mercy
Hospitals & Clinics, Univ. of
Missouri-Kansas City School
of Medicine. *Pulmonary
developmental biology and
mechanisms of lung injury.*



Joan S. Hunt, Ph.D.
University Distinguished
Professor of Anatomy &
Cell Biology, Univ. of Kansas
School of Medicine.
Immunology of pregnancy.



Michael W. Wolfe, Ph.D.
Associate Professor
Molecular and Integrative
Physiology, Univ. of Kansas
School of Medicine. *Gene
regulation in the pituitary
and placenta.*

Kenneth L. Audus

(September 1, 2002 through August 31, 2003)

Professor and Chair of Pharmaceutical Chemistry
University of Kansas
Lawrence, KS
Phone: 785 864-3609
Fax: 785 864-5736
Email: audus@ku.edu

1. Research Interests

Our laboratory is interested in molecular mechanisms controlling placental transport and metabolism; specifically, drugs of abuse, disease and environmental factors and their interactions with mechanisms that regulate the distribution of drugs and drugs of abuse across the maternal-fetal interface; including peptide carriers, organic anion and cation transporters, multidrug resistance efflux mechanisms, and phase I and II enzymes in the trophoblast.

2. Publications (2002-2003)

a. published

Freed, A.L., **Audus, K.L.**, and Lunte, S.M. (2002) Investigation of substance P transport across the blood-brain barrier, *Peptides* 23, 157-165

Hamilton, K.O. and **Audus, K.L.** (2002) Contribution of efflux pump activity to the delivery of pulmonary therapeutics, *Current Drug Metabol.* 3, 1-12

Ampasavate, C., Chandorkar, G.A., VanderVelde, D., Stobaugh, J.F., and **Audus, K.L.** (2002) Transport and metabolism of opioid peptides across BeWo Cells, an *In Vitro* model of the placental barrier, *Int. J. Pharm.* 233, 85-98

Michaelis, M.L., Chen, Y., Hill, S., Reiff, E., Georg, G., Rice, T., and **Audus, K.L.** (2002) Amyloid peptide toxicity and microtubule-stabilizing drugs, *J. Mol. Neurosci.* 19, 101-105

Audus, K.L., Soares, M.J., and Hunt, J.S. (2002) Characteristics of the fetal/maternal interface with potential usefulness in the development of future immunological and pharmacological strategies, *J. Pharmacol. Exp. Ther.* 301, 402-409

Hugger, E.D., **Audus, K.L.**, and Borchardt, R.T. (2002) The Effects of polyethylene glycol on efflux transporters in Caco-2 cell monolayers, *J. Pharm. Sci.* 91, 1980-1990

Hugger, E.D., Novak, B., Burton, P., **Audus, K.L.**, and Borchardt, R.T. (2002) A comparison of commonly used polyethoxylated pharmaceutical excipients on their ability to inhibit P-glycoprotein activity *in vitro*, *J. Pharm. Sci.* 91, 1991-2002

Sinaga E., Jois, S.D., Avery, M., Makagiansar, I.T., Tambunan, U.S., **Audus, K.L.**, and Siahaan, T.J. (2002) Increasing paracellular porosity by E-cadherin peptides: discovery of bulge and groove regions in the EC1-domain of E-cadherin, *Pharm. Res.* 19, 1170-9

Avery, M.L., Meek, C.E., and **Audus, K.L.** (2003) The presence of inducible cytochrome P450 types 1A1 and 1A2 in the BeWo cell line, *Placenta* 24, 45-52

Wimalasena, R., **Audus, K.L.**, and Stobaugh, J.F. (2003) Rapid optimization of the post-column fluorigenic ninhydrin reaction for the HPLC-based derivatization of bradykinin and related fragments, *Biomed. Chromatography* 17, 165-171

Rice, A., Michaelis, M.L., Georg, G., Liu, Y., Turunen, B., and **Audus, K.L.** (2003) Overcoming the blood-brain barrier to taxane delivery for brain tumors and neurodegenerative diseases and brain tumors, *J. Mol. Neurosci.* 20, 339-344

b. in press

Audus, K.L., Hidalgo, I.J., and Borchardt, R.T. (2003) Intestinal Epithelial and Vascular Endothelial Barriers to Peptide and Protein Delivery. In: *Peptide and Protein Drug Delivery* (V. Lee, Ed.), Marcel Dekker, NY, in press

Silverstein, P., Karunaratne, D.N., and **Audus, K.L.** (2003) Utilization of Uptake Studies for Evaluating Activity of Efflux Transporters, *Curr. Protocols Pharmacol.* 00, 000-000

c. abstracts

Young, A.M. and **Audus, K.L.** (2002) Characterization of Efflux Transporters of the Human Trophoblast, Globalization of Pharmaceuticals Education Network Meeting, University of Michigan, Ann Arbor, Michigan

Cooper, J.D., Freed, A.L., **Audus, K.L.**, and Lunte, S.M. (2002) Investigation of Substance P Metabolism using Capillary Electrophoresis with Laser-Induced Fluorescence and Liquid Chromatography with Tandem Mass Spectrometry, Globalization of Pharmaceuticals Education Network Meeting, University of Michigan, Ann Arbor, Michigan

Young, A.M. and Audus, K.L. (2002) Characterization of Efflux Transporters of the Human Trophoblast, *Pharm. Sci.* 4, W5053

Davies, M., Freed, A., Lunte, S., **Audus, K.L.**, and Cooper, J. (2002) Investigation of Substance P Metabolism *In Vitro* and *In Vivo* using Capillary Electrophoresis with Laser-Induced Fluorescence and Liquid Chromatography with Tandem Mass Spectrometry, *Pharm. Sci.* 4, W5040

Audus, K.L. (2003) Identification of Molecular Targets at the Maternal:Fetal Interface for Regulating Drug Therapy in Pregnancy, Molecular Biopharmaceutics Conference, Honolulu, Hawaii

Vasandani, V. and **Audus, K.L.** (2003) Effect of Cyclodextrins on P-glycoprotein Efflux Activity in Bovine Brain Endothelial Cells, Kansas City Area Life Sciences Science Day, Kansas City, Missouri

Karunaratne, N. and **Audus, K.L.** (2003) Assessing the Functionality of Efflux Transporters P-Glycoprotein and MRP1 in BeWo Cells with Fluorescent Substrates, Kansas City Area Life Sciences Science Day, Kansas City, Missouri

Young, A.M. and **Audus, K.L.** (2003) Characterization of Efflux Transporters of the Human Trophoblast, Kansas City Area Life Sciences Science Day, Kansas City, Missouri

Audus, K.L., Rice, A., Michaelis, M.L., Liu, Y., Turunen, B., and Georg, G. (2003) Chemical Approaches to Overcoming Multidrug Resistance at the Blood-Brain Barrier, 5th International Conference on Cerebral Vascular Biology (CVB2003), Amarillo, Texas

d. books, book chapters, and reports

Young, A.M., Fukuhara, A., and **Audus, K.L.** (2002) BeWo cells: An *In Vitro* System Representing the Blood-Placental Barrier. In: *Cell Culture Models of Biological Barriers* (Lear, C.M., Ed.), Harwood Academic Publishers, UK, 337-349

Young, A.M., Allen, C.E., and **Audus, K.L.** (2003) Efflux Transporters of the Placenta, *Adv. Drug Del. Rev.* 55, 125-132

Rice, A., Silverstein, P., and **Audus, K.L.** (2003) Brain Microvessel Endothelial Cell Cultures as *In Vitro* Models to Study the Blood-Brain Barrier. In: *Blood-Spinal and Brain Barriers in Health and Disease* (Sharma, H.S., Ed.), Academic Press, Inc., New York, 47-56

3. Grant Support

National Institutes of Health, “Biology at the Maternal-Fetal Interface”, HD39878, Principal Investigator, Michael J. Soares, \$583,391 (direct costs/year), Total duration of the award: May 1, 2002 through April 30, 2007 [Principal Investigator Subproject II, **Kenneth L. Audus**].

NRSA Fellowship, “Improving Delivery of HIV-1 Protease Inhibitors”, F32 AI10657, Postdoctoral Fellow, Peter Silverstein, \$53,944 (direct costs/year), Total duration of the award: March 1, 2001 through February 28, 2004 [Preceptor, **Kenneth L. Audus**].

NCI, “Taxol-Brain Delivery”, 1 RO1 CA82801-01, Principal Investigator, G.I. Georg, \$177,849 (direct costs/year), Total duration of the award: July 1, 1999 through April 30, 2004 [Co-Investigator, **Kenneth L. Audus**].

American Heart Association, “Molecular Engineering of Plasminogen-Derived Kringles”, Principal Investigator, M. Richter, \$55,000 (direct costs/year), Total duration of the award: July 1, 2001 through June 30, 2003 [Co-Investigator, **Kenneth L. Audus**].

NSF, “Microanalytical Methods for Investigation of Metabolism and Transport of Substance P”, CHE-0111618, Principal Investigator, S. Lunte, \$87,285 (direct costs/year) Total duration of the award: August 15, 2001 through July 31, 2003 [Co-Investigator, **Kenneth L. Audus**].

National Institutes of Health, “Modulation of the intercellular junctions cadherins”, RO1-CA-85917, Principal Investigator, T.J. Siahaan, \$157,500 (direct costs/year), Total duration of the award: July 1, 2001 through June 30, 2005 [Co-Investigator, **Kenneth L. Audus**].

National Institutes of Health, “Analytical Methods for Investigating Peptide Transport”, 1 RO1 NS42929, Principal Investigator, S. Lunte, \$94,388 (direct costs/year), Total duration of the award: March 18, 2002 through January 31, 2007 [Co-Investigator, **Kenneth L. Audus**].

American Foundation for Pharmaceutical Education, Predoctoral Fellow, Amber Young, \$6,000 (direct costs/year), Total duration of the award: September 1, 2003 through August 31, 2004 [Mentor, **Kenneth L. Audus**].

4. Meetings Attended

5th International Conference on Drug Metabolism/Applied Pharmacokinetics, September 2002, Merrimac, Wisconsin

Globalization of Pharmaceutics Education Network Meeting, November 2002, University of Michigan, Ann Arbor, Michigan

American Association of Pharmaceutical Scientists Annual Meeting, November 2002, Toronto, Canada

Molecular Biopharmaceutics Conference, January, 2003, Honolulu, Hawaii (*Sponsored by the Drug Delivery Foundation*)

5th International Conference on Cerebral Vascular Biology (CVB2003), June 2003, Amarillo, Texas

NIDA Sponsored Workshop on Placental Proteins, Drug Transport, and Fetal and Perinatal Development, August 2003, Bethesda, Maryland

5. Committees, Consulting, etc.: National

National

Council Delegate for the Section on Pharmaceutical Sciences, American Association for the Advancement of Science (2002-present)

Member, Scientific Advisory Board, Genzyme Pharmaceuticals (2001-present)

Member, Steering Committee, Kansas City Discussion Group of Pharmaceutical and Allied Sciences (1989-present)

Coordinator, Short Course on Designing Drugs for Delivery to the Brain: The Basic Biological Issues and Current Design Approaches, Sepracor Pharmaceuticals, Marlborough, MA, September 27, 2002

Coordinator, Short Course on Designing Drugs for Delivery to the Brain: The Basic Biological Issues and Current Design Approaches, Eli Lilly, Indianapolis, IN, March 27-28, 2003

6. Journals Refereed

Associate Editor, *Journal of Pharmacology and Experimental Therapeutics*

Editorial Advisory Boards, *Biological & Pharmaceutical Bulletin*; *Current Pharmaceutical Design*; *International Journal of Pharmaceutics*; *Journal of Pharmaceutical Sciences*; *Journal of Pharmacy and Pharmacology*

Ad Hoc Reviewer for:

<i>Brain Research</i>
<i>Brain Research Bulletin</i>
<i>European Journal of Pharmaceutical Sciences</i>
<i>Journal of Controlled Release</i>
<i>Journal of NeuroVirology</i>
<i>Journal of Neuroscience Methods</i>
<i>Journal of Pharmacology and Experimental Therapeutics</i>
<i>Journal of Pharmaceutical Sciences</i>
<i>Journal of Pharmacy and Pharmacology</i>
<i>Life Sciences</i>
<i>Molecular Pharmacology</i>
<i>Peptides</i>
<i>Pharmaceutical Research</i>
<i>Proceedings of the National Academy of Sciences</i>

7. Seminars Presented

- “Transporters and Pharmacokinetic Consequences for Blood-Brain Barrier Penetration,” *5th International Conference on Drug Metabolism/Applied Pharmacokinetics*, Merrimac, Wisconsin, September 2002
- “Blood-Brain and Blood-Fluid Barriers,” *Short Course on Designing Drugs for Delivery to the Brain: The Basic Biological Issues and Current Design Approaches*, Sepracor Pharmaceuticals, Marlborough, Massachusetts, September 2002
- “Overview of *In Vitro/In Vivo* Blood-Brain Barrier Models,” *Short Course on Designing Drugs for Delivery to the Brain: The Basic Biological Issues and Current Design Approaches*, Sepracor Pharmaceuticals, Marlborough, Massachusetts, September 2002
- “Protein Binding, Cytochrome P450, and Efflux Mechanisms: Significance for Brain Penetration,” *Short Course on Designing Drugs for Delivery to the Brain: The Basic Biological Issues and Current Design Approaches*, Sepracor Pharmaceuticals, Marlborough, Massachusetts, September 2002
- “*In Vitro* Models and Drug Transport in the CNS,” *Globalization of Pharmaceutics Education Network*, Ann Arbor, Michigan, November 2002
- “Identification of Molecular Targets at the Maternal:Fetal Interface for Regulating Drug Therapy in Pregnancy,” *Molecular Biopharmaceutics Conference, Sponsored by the Drug Delivery Foundation*, Honolulu, Hawaii, January 2003
- “Blood-Brain and Blood-Fluid Barriers,” *Short Course on Designing Drugs for Delivery to the Brain: The Basic Biological Issues and Current Design Approaches*, Eli Lilly, Indianapolis, Indiana, March 2003
- “Overview of *In Vitro/In Vivo* Blood-Brain Barrier Models,” *Short Course on Designing Drugs*

for Delivery to the Brain: The Basic Biological Issues and Current Design Approaches, Eli Lilly, Indianapolis, Indiana, March 2003

“Protein Binding, Cytochrome P450, and Efflux Mechanisms: Significance for Brain Penetration,” *Short Course on Designing Drugs for Delivery to the Brain: The Basic Biological Issues and Current Design Approaches*, Eli Lilly, Indianapolis, Indiana, March 2003

“Chemical Approaches to Overcoming Multidrug Resistance at the Blood-Brain Barrier,” *Cerebral Vascular Biology Conference (CVB 2003)*, Amarillo, TX, June 2003

“Placental drug metabolism and adaptation to drug exposures in pregnancy,” *National Institute on Drug Abuse Workshop on Placental Proteins, Drug Transport and Fetal and Perinatal Development*, Bethesda, Maryland, August 2003

8. Graduate, Medical, Postdoctoral, and Summer Students

Graduate Students:

Antonie Rice (1996-2002; Ph.D. in Pharmaceutical Chemistry)

Courtnei Allen (2000-2002; M.S. in Pharmaceutical Chemistry)

Amber Young (2000-present) Recipient of an American Foundation for Pharmaceutical Education Predoctoral Fellowship

Erik Rytting (2001-present) Recipient of a Madison and Lila Self Predoctoral Fellowship

Bradley Yops (2001-2003; M.S. in Pharmaceutical Chemistry)

Postdoctoral Fellows:

Dr. Peter Silverstein (2000-present) Recipient of an NIH NRSA Postdoctoral Fellowship

Dr. Veena Vasandani (2002-present)

Dr. Nedra D. Karunaratne nee' (2002-2003; Senior Lecturer in Chemistry, Open University of Sri Lanka)

Dr. Hong Jin (2003-present)

Dr. Claudia Bode (2003-present) Recipient of an Institutional Research and Academic Career Development Award (IRACDA) Postdoctoral Fellowship

Summer Students:

Ryan Van Maanen, (Summer 2002; from Central College, Iowa)

Jordon Bryan, (Summer 2003; from Oklahoma State University)

Courtney Tritle, (Summer 2003; from the University of South Dakota)

9. Research Associates, Assistants, Technicians and Aides

Dr. Catharina A. Holm, visiting Fulbright Scholar, South Africa (2001-2002; Ph.D. 2003)

Magan Pearson, Laboratory Technician, (2002)

Davani Khosoro, visiting scholar, M.S. Pharmacist, Royal Danish School of Pharmacy (2002)

Maria Anderberg, visiting scholar, M.S. Pharmacist from the Royal Danish School of Pharmacy (2003)

Fride Iversen, visiting scholar, M.S. Pharmacist, Royal Danish School of Pharmacy (2003)

Alan R. Godwin

(September 1, 2002 through August 31, 2003)

Assistant Professor
Department of Molecular and Integrative Physiology
University of Kansas Medical Center
3901 Rainbow Boulevard
Kansas City, KS 66160
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Fax: 913 588-7430
Email: agodwin@kumc.edu

1. Research Interests

Hox genes are evolutionarily conserved transcription factors that are important in determining changes along the major anterior-posterior axis in animals as diverse as flatworms, fruit flies, and man. Targeted mutations in the mouse Hox genes often mimic aspects of human birth defects. Little is understood about how these genes carry out this process, especially which genes are regulated by these transcription factors. Hence, increased understanding of the basic biology of Hox genes may eventually aid understanding of the underlying causes of some birth defects. The Godwin laboratory is pursuing detailed examination of the interacting partners and the genes controlled by Hoxc13, a model of some human ectodermal dysplasias. Pups born to female Hoxc12 mutant mice die within a few days after birth due to uterine conditions. We are using these mice as a model to examine the role of Hox genes in uterine control of fetal development.

2. Publications (2002-2003)

a. abstracts

R. Thummel, Li, L., Sarras, M. P., Jr., and **Godwin, A. R.** (2002) Hoxc13 Orthologs in Zebrafish *Dev. Biol.* 247: 445.

3. Grant Support

NIH/NIAMS, "Hoxc13 and Hair Follicle Morphogenesis", Principal Investigator, **Alan R. Godwin**. \$188,000 (direct costs/year), Total duration of the award: August 1, 2000 through July 31, 2005.

National Institutes of Health, "Biology at the Maternal-Fetal Interface", HD39878, Principal Investigator, Michael J. Soares, \$583,391 (direct costs/year), Total duration of the award: May 1, 2002 through April 30, 2007 [Co-Investigator, **Alan R. Godwin**].

National Institutes of Health/NHLBI, "Locus-linked Regulatory Motifs of Globin Gene Switching," RO1 HL67336, Principal Investigator, **Kenneth R. Peterson**, \$225,000 (direct costs/year), Total duration of the award: June 15, 2001 through May 31, 2005 [Co-Investigator, **Alan R. Godwin**].

Hall Family Foundation, "Isolation of a Novel Gene from a Mouse Model of Ectodermal Dysplasia", Co-Principal Investigator, R. A. White, \$50,000 (direct costs/year), Total duration of the award: September 1, 2002 through August 31, 2003 [Co-Principal Investigator, **Alan R. Godwin**].

KUMC/KBRIN, "Role of Matrix Metalloproteinases in Tissue Regeneration", Principal Investigator, M. P. Sarras, Jr., \$25,000 (direct costs/year), Total duration of the award: April 1, 2002 through March 31, 2003 [Co-Investigator, **Alan R. Godwin**].

4. Meetings Attended

43rd Annual Midwest Developmental Biology Meeting & Singer Symposium, June 7-10, 2003, Stowers Institute for Medical Research, Kansas City, Missouri (*member-organizing committee*)

5. Journals Refereed

Member of 2003 Editorial Board, *Developmental Dynamics*

Ad Hoc Reviewer for:

<i>Developmental Biology</i>
<i>Developmental Dynamics</i>
<i>Genesis</i>
<i>Journal of Investigative Dermatology</i>
<i>Naturwissenschaften</i>

6. Seminars Presented

"Hoxc12: a reproductive phenotype?" Center for Reproductive Sciences, KUMC, February 2003

"Hoxc13 and ectodermal appendages" Division of Biology, Kansas State University, Manhattan, Kansas, April 2003

"Hoxc13: "Hair today, gone tomorrow"" Center for Human Molecular Genetics, University of Nebraska Medical Center, Omaha, Nebraska, May 2003

7. Graduate, Medical, Post-doctoral, and Summer Students

Graduate Students:

Ryan Thummel
Peizhen Song

Summer Students:

Dominik Choromanski, Medical Student (Poland), Summer Research
Kara Wagoner, Rotation Student
Brian Chase, Summer Student (Undergraduate)
Nelson Stauffer, Summer Student (High School)

8. Research Associates, Assistants, Technicians, and Aides

Martin Perry, Research Assistant
Judy Dunmore, Senior Research Associate

Leslie L. Heckert

(September 1, 2002 through August 31, 2003)

Associate Professor
Department of Molecular and Integrative Physiology
University of Kansas Medical Center
3901 Rainbow Boulevard
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Fax: 913 588-7430
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1. Research Interests

Our research focuses on understanding the transcriptional and cell-signaling processes important for gonadal function and development. We are currently studying the genes that encode the FSH receptor (FSHR), a protein expressed only in somatic cells of the gonads, steroidogenic factor 1 (SF-1), an orphan nuclear receptor required for gonad and adrenal formation, and DMRT1, an evolutionarily conserved gene that regulates testis differentiation. Through the characterization of these genes, we hope to identify key regulatory proteins important for gonadal development and Sertoli cell-specification. Recently, we have developed mouse models that express SF-1 only from a YAC transgene. Using this technology, we will explore the physiological relevance of SF-1's functional domains. Transgenic mice are used to help confirm regulatory regions *in vivo* and to generate mouse models for Sertoli cell function.

2. Publications

a. published

Scherrer, S.P., Rice, D.A. and **Heckert, L.L.** (2002) "Expression of steroidogenic factor 1 in the testis requires an interactive array of elements within its proximal promoter" *Biology of Reproduction* 67, 1509-1521

b. in press

Lei N and **Heckert, L.L.** "GATA4 regulates testis expression of the doublesex and mab-3 related transcription factor *Dmrt1*", *Molecular and Cellular Biology*, in press

c. abstracts

Heckert, L.L., Scherrer, S.P., Presley, J.J. (2003) "A 550 Kb Ftz-F1-containing yeast artificial chromosome rescues the gonadal and adrenal defects that develop in SF-1 knockout mice." The XVII Testis Workshop, Phoenix, Arizona

Hermann, B.P., Hornbaker, K.I., **Heckert, L.L.** (2003) “Ftz-f1-Associated transcript (Fat) is a novel gene that co-expresses with Steroidogenic factor-1.” 85th Annual Meeting of the Endocrine Society, Philadelphia, Pennsylvania

d. book in press

Heckert, L.L. (2003) “Structure & Regulation of the FSH Receptor Gene” in *The Sertoli Cell* (M.D Griswold and M.K. Skinner eds.) Academic Press, **in press**

3. Grant Support

National Institutes of Health/NICHD, “The Center for Reproductive Sciences – Project 1, Regulation of SF1 in the Gonads”, Principal Investigator, Leslie L. Heckert (Co-investigator, Kenneth R. Peterson), \$121,471 (direct costs/year), Total duration of the award: April 1, 2001 through March 31, 2006.

National Institutes of Health/NICHD, “Hormonal and cell-specific regulation of Dmrt1”, R01 HD41056, Principal Investigator, Leslie L. Heckert, \$202,500 (direct costs/year), Total duration of the award: August 1, 2002 through July 31, 2007.

SELF Faculty Scholar Award, University of Kansas, Principal Investigator, Leslie L. Heckert. \$50,000/yr. Total duration of the award: July 1, 2000 through June 30, 2003.

G3201240 NASA “Long-term simulated microgravity inhibits spermatogenesis in adult male rats”, Principal Investigator, Joseph Tash, \$210,854 (total costs/year), Total duration of the award: July 1, 2001 through June 30, 2003 [Co-Investigator, **Leslie Heckert**].

KU Medical Center Research Institute. “A functional role for Dmrt1 in testis development,” Principal Investigator, Leslie L. Heckert, total award \$35,000, Total duration of the award: February 10, 2001 through January 31, 2003.

4. Meetings Attended

The XVII Testis Workshop, March 2003, Phoenix, Arizona

American Society of Andrology Annual Meeting, March 2003, Phoenix, Arizona

85th Annual Meeting of the Endocrine Society, June 2003, Philadelphia, Arizona

5. Journals Refereed

Member, Editorial Board, Molecular Endocrinology

Member, Editorial Board, Journal of Andrology

Ad hoc reviewer for:

<i>Ad hoc reviewer for Endocrinology</i>
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<i>Ad hoc reviewer for Biology of Reproduction</i>
--

6. Committees, Consulting, etc.: National

Member NIH/NICHD U54 Review Committee, November 2002

Ad hoc reviewer for National Institutes of Health BCE study section June 2003

Chairperson for Session I: Germ Cell Development March 2003, The XVII Testis Workshop, Phoenix, Arizona

Member, planning committee for 2004 Testis Workshop

Member, planning committee for 2003 Annual meeting for the Society for the Study of Reproduction

7. Seminars Presented

"GATA4 regulates testis-specific expression of the doublesex and mab-3 related transcription factor Dmrt1", Johns Hopkins University, Baltimore, Maryland, November 2002

"Transcriptional regulation of the *Ftz-F1* gene" *SCCPRR Research Meeting, Reproductive Sciences Branch and Center for Population Research, National Institutes of Health, Bethesda Maryland, May 2003*

8. Honors

Self Faculty Scholar Award; Awarded June 2000. Term from July 2000-June 2003

KUMC Faculty Scholar Award

9. Graduate, Medical, Post-doctoral, and Summer Students

Graduate Students:

Ning Lei (2000-present)

Brian Hermann (2000-present)

Postdoctoral Fellows:

Rengasamy R. ManiMaran, Ph.D. (2002-present)

Tatiana Karpova, Ph.D. (2003-present)

10. Research Associates, Assistants, Technicians and Aides

Daren Rice, Research Associate (1998-present)

Jeremy Presley, Research Assistant (2001-2003)

Kaori Iha-Hornbaker, Research Assistant (2002-present)

Joan S. Hunt

(September 1, 2002 through August 31, 2003)

Senior Associate Dean for Research and Graduate Education, School of Medicine
University Distinguished Professor
Department of Anatomy and Cell Biology
University of Kansas Medical Center
3901 Rainbow Blvd.
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Email: jhunt@kumc.edu

1. Research Interests

Our focus is on immunological aspects of pregnancy. In order to understand how semiallogeneic embryos are protected against maternal immune cells and their products, we study macrophages in the uterus and placenta and the expression, regulation and functions of placental transplantation antigens (HLA). The results of these experiments on the natural situation of pregnancy might be applicable to other conditions such as artificial transplants where protection against immune cell activity would be desirable.

Limited recognition of the semiallogeneic fetus by the maternal immune system has beneficial effects on fertility and maintenance of pregnancy. We are studying one product of activated immune cells, the multifunctional polypeptide growth factor, tumor necrosis factor, and other members of this supergene family that might be among the "recognition signals" that contribute to successful pregnancy.

2. Publications (2002-2003)

a. published

Petroff, M.G., Chen, L., Phillips, T.A., and **Hunt, J.S.** (2002) B7 family molecules: novel immunomodulators at the maternal-fetal interface. *Placenta* 23, Supplement A, *Trophoblast Res.* 16, S95-S101

Audus, K.L., Soares, M.J. and **Hunt, J.S.** (2002) Characteristics of the fetal/maternal interface with potential usefulness in the development of future immunological and pharmacological strategies. *J. Pharmacol. Exp. Therapeut.* 301, 402-409

Burnett, T.G., Tash, J.S. and **Hunt, J.S.** (2002) Investigation of the role of NOS-2 in mouse pregnancy using mutant mice. *Reproduction* 124, 49-57

Langat, D.K., Morales, P. J., Fazleabas, A.T., Mwenda, J.M. and **Hunt, J.S.** (2002) Baboon placentas express soluble and membrane-bound Paan-AG proteins encoded by alternatively

spliced transcripts of the class Ib major histocompatibility complex gene, *Paan-AG*. *Immunogenet.* 54, 164-173

Petroff, M.G., Sedlmayr, P., Azzola, D., and **Hunt J.S.** (2002) Decidual macrophages are potentially susceptible to inhibition by class Ia and class Ib HLA molecules. *J. Reprod. Immunol.* 56, 3-17

Langat, D.K., and **Hunt J. S.** (2002) Do non-human primates comprise appropriate experimental models for studying the function of HLA-G? *Biol. Reprod.* 67, 1367-1374

Gill, R.M., Ni, J. and Hunt J.S. (2002) Differential expression of LIGHT and its receptors in human placentas and amniochorion membranes. *Amer. J. Pathol.* 161, 2011-2017

Petroff, M.G., Chen, L., Morgan, K.A., Phillips, T.A., Azzola, D., Sedlmayr, P., and **Hunt J.S.** (2003) B7 family molecules are favorably positioned at the human maternal fetal interface. *Bio. Reprod.* 68, 1496-1504

Gill, R.M., Ka, H. and **Hunt J.S.** (2003) TRAIL, LIGHT and the expanding tumor necrosis factor superfamily in human placentas. *Proc. Indian Nat. Acad. Sci.* B69 (2), 41-53

Robertson, S.A., Redman, C.W., McCracken, S A., **Hunt, J.S.**, Dimitriadis, E., Moffett-King, A. and Chamley, L. (2003) Immune modulators of implantation and placental development. *Trophoblast Res.* 17, S16-S20

Ka, H., and **Hunt, J.S.** (2003) Temporal and spatial patterns of expression of inhibitors of apoptosis (IAP) in human placentas. *Am. J. Pathol.* 163, 413-422

Phillips, T. A., Ni, J. and **Hunt, J.S.** (2003) Cell-specific expression of B lymphocyte- (APRIL, BLYS) and Th2- (CD30L/CD153) promoting tumor necrosis factor superfamily ligands in human placentas. *J. Leukocyte Biol.* 74, 81-87

Hunt, J.S., Pace, J. L., Morales, P. J. and Ober, C. (2003) Immunogenicity of the soluble isoforms of HLA-G. *Mol. Human Reprod.* 9, 729-735

b. in press

Morales, P., Pace, J.L., Platt, J.S., Phillips, T.A., Morgan, K., Fazleabas, A.T. and **Hunt, J.S.** Placental cell expression of HLA-G2 isoforms is limited to the invasive trophoblast phenotype. *J. Immunol.*, in press.

c. abstracts

Ka, H., Phillips, T.A. and **Hunt, J.S.** (2002) TRAIL increases IGF-II expression in human cytotrophoblast. Soc. Gynecological Investigation Annual Meeting, Los Angeles, California

Gill, R.M., Ni, J. and **Hunt, J.S.** (2002) Localization of the TNF superfamily member, LIGHT, and its TNFR superfamily member receptors, HVEM, LT β R and DcR3/TR6, in the human placenta. Soc. Gynecological Investigation Annual Meeting, Los Angeles, California

Langat, D.K., Morales, P.J., Fazleabas, A.T., Mwenda, J.M. and **Hunt, J.S.** (2002) Baboon placentas express alternatively spliced transcripts and proteins encoded by the non-classical MHC gene, *Paan-AG*. Am. Soc. Immunol., New Orleans, Louisiana

Hunt, J.S. (2002) Reproductive Immunology in Transition: Cellular and molecular trends. 8th Meeting of the International Federation of Placenta Associations, Melbourne, Australia.

Phillips, T.A., Gill, R., Ka, H. and **Hunt, J.S.** (2002) The TNF superfamily and pregnancy: support for a Th2 bias. TNF Superfamily Conference 2002, San Diego, California

d. books, book chapters published

Hunt, J.S. Major histocompatibility antigens in reproduction (2002) In: *The Endometrium*, Chapter 26. S. Glasser, J. Aplin, L. Giudice and S. Tabibzadeh, Eds. Taylor & Francis, London and New York. P. 405-415.

Hunt, J.S. Immunogenetics: genetic regulation of immunity in pregnancy (2002) In: *Reproductive Medicine: Molecular, Cellular and Genetic Fundamentals*. B.C.J.M. Fauser, Ed. Parthenon Press, New York, NY. Chapter 9, pp. 153-167.

Hunt, J.S. and Petroff, M.G. Placental Immunology (2003) In: *Encyclopedia of Hormones*. H.L. Henry and A.W. Norman, Eds. Academic Press, NY. Vol. 3:224-231.

Hunt, J.S. The influence of pregnancy on cytokine production (2003) In: *Bile Acids and Pregnancy*. Leuschner et al.(Eds). Kluwer Academic Publishers, Lancaster, U.K. PP. 17.

Hunt, J.S. (2003) Introduction: Symposium in honor of Y. W. (Charlie) Loke, Immunobiology of Pregnancy. *Trophoblast Res.* 17:S3 (*Placenta*, 24, Supplement A).

3. Grant Support

National Institutes of Health, “Decidual Cell/Placental Interactions”, 5RO1 HD24212, Principle Investigator, Joan S. Hunt, \$1,277,405 (direct + indirect costs), Total duration of the award: August 1, 1999 through July 30, 2003; No cost extension to July 30, 2004.

National Institutes of Health, Project IV, “TRAIL and the Human Implantation Site”, 2U54 HD33994-06, Principle Investigator, Joan S. Hunt, \$845,008 (direct + indirect costs), Total duration of the award: April 23, 2001 through January 3, 2006.

National Institutes of Health, “Biology at the Maternal-Fetal Interface” PO1 HD39878, Principle Investigator, Michael J. Soares, Principle Investigator Project III, Joan S. Hunt, “Class I MHC Gene Expression by Human Trophoblast Cells”, \$890,441/\$1,335,661 and Core B Director, Joan S. Hunt, \$301,922/\$452,884, Total duration of the award: May 1, 2002 through April 30, 2007.

National Institutes of Health, “Kansas Biomedical Research Infrastructure Network”, 1 P20 RR16475-01 NCCR RFA, Principle Investigator, Joan S. Hunt, \$5,900,000 (direct + indirect costs), Total duration of the award: July 1, 2001 through June 30, 2004.

National Institutes of Health, “Kansas BRIN Supplement”, 3 P20 RR016475-03S1, Principle Investigator, Joan S. Hunt, \$1,892,000 (direct + indirect costs), Total duration of the award: October 15, 2002 through October 14, 2004.

National Institutes of Health, “Kansas BRIN Administrative Supplement”, 3 P20 RR016475, Principle Investigator, Joan S. Hunt, \$438,229 (direct + indirect costs), Total duration of the award: September 1, 2001 through August 31, 2004.

CONRAD Program for Contraceptive Research & Development (CICCR), “*Paan-AG* as a contraceptive target in baboons”, Principle Investigator, Joan S. Hunt, \$175,0000, Total duration of the award: September 1, 2001 August 31, 2002; \$162,082, Total duration of the award: September 1, 2002 August 31, 2003.

National Institutes of Health, “Pregnancy-specific Modulation of Natural Killer Cells”, 1RO1 HD37123-01, Michael J. Soares, \$168,348/year (direct costs/year), Total duration of the award: August 1, 1999 through July 30, 2002 [Co-Investigator, **Joan S. Hunt**].

National Institutes of Health, U54 Reproductive Sciences Center Grant; Principle Investigator, Paul F. Terranova, \$1,124,250 (direct costs), Total duration of the award: April 23, 2001 through March 31, 2006 [Associate Director and Director, Cell and Tissue Culture Core: Joan S. Hunt].

KUMC Training Program in Biomedical Research, Principle Investigator, Joan S. Hunt, \$670,034, Total duration of the award: July 1, 1999 through June 30, 2002; renewed June 1, 2002 through June 30, 2003.

KUMC Research Institute Bridging Grant “Class I MHC Genes in Human Trophoblast Cells”, Principle Investigator, Joan S. Hunt, \$24,998.56, Total duration of the award: June 1, 2001 through May 31, 2002.

4. Meetings Attended

35th Annual Meeting, Society for the Study of Reproduction, August 2002, Baltimore, Maryland (Organizer and Chairperson)

8th International Federation of Placenta Associations, October 2002 Melbourne, Australia (Chairperson, Symposium in honor of Y.W. Loke, and Organizing Committee)

International Federation of Placenta Associations Annual Meeting, September 2002, Melbourne, Australia (Organizing Committee)

10th Meeting of the European Placenta Group, 2003, Mainz, Germany (Organizing Committee, R. Leiser, Organizer)

Placenta Association of the Americas and International Federation of Placenta Associations, September 2004, Alvarado, California (Organizing Committee)

Indo/US Workshop, “Cell Mediated Immunology of the Female Reproductive Tract”, February 2002, New Delhi, India

The Population Council, “HLA gene regulation: a critical aspect of placental immune privilege”
April, 2002, Rockefeller University

NICHD Intramural program, “Placental HLA and Tolerance in Pregnancy” April 2002
(J. Zhang, host)

Workshop on Bile Acids in Pregnancy - Falk Workshop, “The influence of pregnancy on
cytokine production” June 2002, Freiburg, Germany

Serono Symposium on “Embryo Implantation – Cellular Changes from Bench to Bedside”
July 2002, Uncasville, Connecticut

35th Annual Meeting, Society for the Study of Reproduction, “The TNF Supergene Family:
Potential Functions in Human Placentas”, Minisymposium, July 2002

Kansans Come Together Under the K-BRIN: A Researcher-Focused Program, Principle
Investigator, Biomedical Research Infrastructure Network programs, National Center for
Research Resources, August 2002

Kansans Come Together Under the K-BRIN: A Researcher-Focused Program, National
Advisory Council, National Center for Research Resources, September 2002

8th Meeting of the International Federation of Placenta Associations, “Reproductive
Immunology in Transition: Cellular and Molecular Trends”, October 2002, Melbourne,
Australia (Plenary Speaker)

“Investigations of Soluble HLA-G, a Potential Modulator of Immune and Other Cells During
Pregnancy”, Satellite Symposium, October 2002, Newcastle, Australia

International Federation of Placenta Associations, October 2002, Melbourne, Australia
Workshop presentation

1st Mediterranean Congress on Reproductive Medicine, November 2002, Taormina, Sicily

CONRAD/CICCR/WHO Conference, May 2003, Bellagio, Italy

5. Journals Refereed

1997-pres. Editor-in Chief, *Journal of Reproductive Immunology*

1999-pres. Editorial Board, *Biology of Reproduction*

Ad Hoc Reviewer for:

<i>Alcoholism: Clinical and Experimental Research</i>	<i>Immunopharmacology</i>
<i>American Journal of Obstetrics and Gynecology</i>	<i>Molecular and Cellular Endocrinology</i>
<i>American Journal of Pathology</i>	<i>Molecular Human Reproduction</i>
<i>American Journal of Physiology</i>	<i>New England Journal of Medicine</i>
<i>American Journal of Reproductive Immunology</i>	<i>Journal of Clinical Endocrinology & Metabolism</i>
<i>Anatomical Record</i>	<i>Journal of Cellular Physiology</i>
<i>Arthritis & Rheumatism</i>	<i>Journal of Clinical Investigation</i>

<i>Biochimica et Biophysica Acta</i>	<i>Journal of Gynecological Investigation</i>
<i>Biology of Reproduction</i>	<i>Journal of Immunology</i>
<i>BioTechniques</i>	<i>Journal of Leukocyte Biology</i>
<i>Cellular Immunology</i>	<i>Journal of Molecular & Cellular Cardiology</i>
<i>Critical Reviews in Immunology</i>	<i>Journal of Reproductive Immunology</i>
<i>Cytokine</i>	<i>Laboratory Investigation</i>
<i>Developmental Biology</i>	<i>Life Sciences</i>
<i>Diabetes</i>	<i>Molecular Human Reproduction</i>
<i>Endocrine</i>	<i>Oncology Research</i>
<i>Endocrine J.</i>	<i>Pediatric Research</i>
<i>Endocrinology</i>	<i>Placenta</i>
<i>Endotoxin Research</i>	<i>Prostaglandins</i>
<i>European Journal of Cancer</i>	<i>Reproduction</i>
<i>Experimental Cell Research</i>	<i>Fertility and Development</i>
<i>Fertility and Sterility</i>	<i>Regional Immunology</i>
<i>Human Immunology</i>	<i>The New England Journal of Medicine</i>
<i>Human Reproduction</i>	<i>Trophoblast Research</i>
<i>Immunogenetics</i>	<i>Immunology Letters</i>
<i>Immunology</i>	<i>Proceedings of the National Academy of Science USA</i>

6. Committees, Consulting, etc.: National

Ad hoc reviewer, Americas Fellowships, J. Strauss, Chairman (2002)

Centocor, Inc. Consultant (2002)

Member, NCRP Council

7. Seminars Presented

“Research Careers in Academia”, Student Research Forum, KUMC, Kansas City, Kansas, 2002

“Critical Features of Funded Grants”, Women in Medicine & Faculty Development, KUMC, Kansas City, Kansas, 2002

“Immune Mechanisms in Pregnancy: Antibodies, Complement and Cytokines”, 35th Annual Meeting, Society for the Study of Reproduction, Baltimore, Maryland, July 2002 (Organizer and Chairperson, Minisymposium)

Symposium in honor of Y.W. Loke, and Organizing Committee, 8th International Federation of Placenta Associations, Melbourne, Australia, October 2002 (Chairperson)

“10th Meeting of the European Placenta Group”, Mainz, Germany, 2003 (Organizing Committee, R. Leiser, Organizer)

“Cell Mediated Immunology of the Female Reproductive Tract”, Indo/US Workshop, New Delhi, India, February 2002

“HLA gene regulation: a critical aspect of placental immune privilege”, *The Population*

Council, Rockefeller University, April 2002

“Placental HLA and Tolerance in Pregnancy”, *NICHD Intramural program*, April 2002

“The influence of pregnancy on cytokine production”, *Workshop on Bile Acids in Pregnancy – Falk Workshop*, Freiburg, Germany, June 2002

“Immune Cells in the Human Uterus – Role in Implantation”, *Serono Symposium on “Embryo Implantation- Cellular Changes from Bench to Bedside”*, Uncasville, Connecticut, July 2002

“The TNF Supergene Family: Potential Functions in Human Placentas”, *Minisymposium, 35th Annual Meeting, Society for the Study of Reproduction*, July 2002

“Kansans Come Together Under the K-BRIN: A Researcher-Focused Program”, *Principle Investigator, Biomedical Research Infrastructure Network programs, National Center for Research Resources*, August 2002

“Kansans Come Together Under the K-BRIN: A Researcher-Focused Program”, *National Advisory Council, National Center for Research Resources*, September 2002

“Reproductive Immunology in Transition: Cellular and Molecular Trends”, *Plenary Speaker, 8th Meeting of the International Federation of Placenta Associations*. Melbourne, Australia, October 2002

“Investigations of Soluble HLA-G, a Potential Modulator of Immune and Other Cells During Pregnancy”, *Satellite Symposium, Newcastle, Australia*, October 2002

“TRAIL Increases IGF-II Expression in Human Cytotrophoblast”, H. Ka, Phillips, T.A. and Hunt, J. S. *Workshop presentation, International Federation of Placenta Associations, Melbourne, Australia*, October 2002

“Soluble HLA-G and Immunity in Pregnancy”, *Monash University, Melbourne, Australia*, October, 2002

“HLA and the Maternal-Fetal Immunological Relationship”, *1st Mediterranean Congress on Reproductive Medicine*, Taormina, Sicily, November 2002

“Paan-AG as a Contraceptive Target in Baboons”, *CONRAD/CICCR/WHO Conference*, Bellagio, Italy, May 2003

“HLA-G at the Maternal-Fetal Interface”, *University of Chicago, Chicago, Illinois*, June 2003

8. Honors

2002 Doctor of Science *honoris causa*, University of Guelph, Canada

2002 Top Ten Researcher, KUMC Research Institute, Inc.

2002 Beacon Award, Frontiers in Reproduction, Marine Biology Laboratory

2003 Associate Marshal, KUMC (declined)

9. Graduate, Medical, Postdoctoral, and Summer Students

Graduate Students (*completed):

1997-2002 *Tim Burnett, Ph.D., Dept. of Anatomy & Cell Biol. (KHF Scholar; Biomedical Training Grant Scholar)
1999-2002 *Daudi Langat, Ph.D., University of Nairobi, Kenya
1999-2003 *Ryan Gill, PhD candidate (M.D./Ph.D. program, Sutton Scholar)
2000-pres. Ramsey McIntire, Ph.D. candidate, Dept. of Anat. & Cell Biol.

Postdoctoral Fellows:

1998-2003 Margaret Petroff, Ph.D. (NICHD Training Grant fellow; NRSA awardee)
Present: Research Assistant Professor, Dept. of Anat. & Cell Biol., KUMC
2001-pres. Hakhyung Ka, Ph.D.
Present: Post-doctoral fellow, Dept. of Anat. & Cell Biol., KUMC
2002-pres. Daudi Langat, PhD
Present: Post-doctoral fellow, Dept. of Anat. & Cell Biol., KUMC

Summer Students:

10. Research Associates, Assistants, Technicians and Aides

Karen Rodriguez, Administrative Assistant (2002-present)

Kenneth R. Peterson

(September 1, 2002 through August 31, 2003)

Professor of Biochemistry and Molecular Biology
University of Kansas Medical Center
Kansas City, KS 66160
Phone: 913 588-6907
Fax: 913 588-7440
Email: kpeterson@kumc.edu

1. Research Interests

Our laboratory is interested in understanding the molecular mechanisms controlling β -like globin gene switching, particularly the transactivation or pharmacologic induction of fetal γ -globin synthesis and the *cis*-control of globin gene expression during development, including the identification and characterization of DNA elements regulating globin synthesis via interaction of these sequences with trans-acting proteins.

2. Publications (2002-2003)

a. published

Navas, P. A., Li, Q., **Peterson, K. R.**, Swank, R. A., Rohde, A., Roy, J., and Stamatoyannopoulos, G. (2002) Activation of the β -like globin genes is dependent on the presence of the β -locus control region. *Human Mol. Genet.* 11, 893-903

Harju, S. J., McQueen, K. J., and **Peterson, K. R.** (2002) Chromatin structure and control of β -like globin gene switching. *Exptl. Biol. Med.* 227, 683-700

Li, Q., **Peterson, K. R.**, Fang, X., and Stamatoyannopoulos, G. (2002) Locus control regions. *Blood* 100, 3077-3086

Peterson, K. R. (2003) Transgenic mice carrying yeast artificial chromosomes. *Expert Rev. Molec. Med.* 5, 1-25

b. in press

Peterson, K. R., Fedosyuk, H., Nakamoto, B., Rohde, A., Yannaki, E., Stamatoyannopoulos, G., Ciciotte, S., Peters, L. L., Scott, L. M., and Papayannopoulou, T. (2003) Transgenic Cre expression mice for generation of erythroid-specific gene alterations. *Genesis* (Accepted with revision).

Rodova, M., Islam, M. R., **Peterson, K. R.**, and Calvet, J. P. (2003) Remarkable sequence conservation of a small intron in the PKD1 gene. *Mol. Biol. Evol.* (In press).

Navas, P. A., Swank, R., Yu, M., **Peterson, K. R.**, and Stamatoyannopoulos, G. (2003) Mutation of a GT motif in the HS3 core element of the β -globin locus control region: Evidence for developmental stage-specific role of GT6 on globin gene expression. *Human Mol. Genet.* (In press).

c. abstracts

Peterson, K. R., Harju, S., Navas, P. A., and Stamatoyannopoulos, G. (2002) Role of γ -globin gene silencing and chromatin sub-domains in globin gene switching. *Blood* 100:47a. Annual Meeting of the American Society of Hematology, Philadelphia, Pennsylvania

Peterson, K. R., Harju, S., Navas, P. A., and Stamatoyannopoulos, G. (2002) Role of γ -globin gene silencing and chromatin sub-domains in globin gene switching. *Blood Cells, Molecules & Diseases* (In press). Thirteenth Conference on Hemoglobin Switching, Oxford, United Kingdom (in press)

Harju, S., Navas, P. A., Stamatoyannopoulos, G., and **Peterson, K. R.** (2002) Role of γ -globin gene silencing and chromatin sub-domains in globin gene switching. *Blood Cells, Molecules & Diseases* (In press). Thirteenth Conference on Hemoglobin Switching, Oxford, United Kingdom (in press)

Harju, S., McQueen, K. J., Fedosyuk, H., and **Peterson, K. R.** (2002) Deletion of LCR 5'HS4 does not markedly affect β -like globin gene expression in β -YAC transgenic mice. *Blood Cells, Molecules & Diseases* (In press). Thirteenth Conference on Hemoglobin Switching, Oxford, United Kingdom (in press)

Peterson, K. R., Yan, J., Navas, P. A., and Blau, C.A. (2002) Establishment of CID-dependent progenitor cell lines from β -YAC transgenic mice. *Blood Cells, Molecules & Diseases* (In press). Thirteenth Conference on Hemoglobin Switching, Oxford, United Kingdom (in press)

Navas, P. A., Swank, R., **Peterson, K. R.**, and Stamatoyannopoulos, G. (2002) Mutation of a GT motif in the HS3 core element in transgenic mice: Evidence for stage-specific role of GT6 in ϵ - and γ -globin gene expression during development. *Blood Cells, Molecules & Diseases* (In press). Thirteenth Conference on Hemoglobin Switching, Oxford, United Kingdom (in press)

d. books, book chapters published

Peterson, K. R. (2003) Hemoglobin switching: New insights. *Curr. Opin. Hematol.* 10, 123-129.

3. Grant Support

National Institutes of Health/NHLBI, "Locus-linked Regulatory Motifs of Globin Gene Switching," RO1 HL67336, Principal Investigator, **Kenneth R. Peterson**, \$225,000 (direct costs/year), Total duration of the award: June 15, 2001 through May 31, 2005.

National Institutes of Health/NIDDK, “Molecular Control of Fetal γ -globin Gene Expression,” RO1 DK61804, Principal Investigator, **Kenneth R. Peterson**, \$200,000 (direct costs/year), Total duration of the award: September 30, 2001 through May 31, 2005.

Self Faculty Scholar Award - Madison and Lila Self Graduate Fellowship, “Studies of β -like Globin Gene Switching,” Principal Investigator, **Kenneth R. Peterson**, \$50,000 (direct costs/year), Total duration of the award: July 1, 2001 through June 30, 2004.

National Institutes of Health/NHLBI, “Regulation of Globin Gene Switching in Human ES Cells,” RO1 HL067336-03S1 supplement, Principal Investigator, **Kenneth R. Peterson**, \$50,000 (direct costs/year), Total duration of the award: September 22, 2003 through May 31, 2005.

National Institutes of Health/NIDDK, “Kansas Interdisciplinary Center for PKD Research - Project 3, Polycystin G-protein Signal Transduction,” P50 DK57301, Principal Investigator, James P. Calvet, Co-investigator, **Kenneth R. Peterson**, \$144,567 (direct costs/year), Total duration of the award: September 30, 1999 through August 31, 2005.

National Institutes of Health/NIAMS, “*Hoxc13* and Hair Follicle Morphogenesis,” RO1 AR47233, Principal Investigator, Alan R. Godwin, Co-investigator, **Kenneth R. Peterson**, \$188,000 (direct costs/year), Total duration of the award: August 1, 2000 through June 30, 2005

National Institutes of Health, “The Center for Reproductive Sciences – Project 1, Regulation of SF1 in the Gonads,” Principal Investigator, Leslie L. Heckert, Co-investigator, **Kenneth R. Peterson**, \$144,398 (direct costs/year), Total duration of the award: April 1, 2001 through March 31, 2006

National Institutes of Health/NIDDK, “A Mouse Model of Acrodermatitis Enteropathica,” RO1 DK63975, Principal Investigator, Glen K. Andrews, Co-investigator, **Kenneth R. Peterson**, \$250,000 (direct costs/year), Total duration of the award: April 1, 2003 through January 31, 2008.

4. Meetings Attended

Annual Meeting of the American Society of Hematology, 2002, Philadelphia, PN

Thirteenth Conference on Hemoglobin Switching, 2002, Oxford, UK

5. Journals Refereed

Ad Hoc Reviewer for:

<i>Bio Techniques</i>
<i>Blood</i>
<i>EMBO Journal</i>
<i>Genomics</i>
<i>Journal Biological Chemistry</i>

6. Committees, Consulting, etc.: National

Ad hoc reviewer, NIH MBRS SCORE Program grant, 2002-2003.

Ad hoc reviewer, Muscular Dystrophy Campaign grant, 2003.

Ad hoc member, NIH Hematopoiesis (HP) Study Section, 2003

7. Seminars Presented

“Role of γ -globin gene silencing and chromatin sub-domains in globin gene switching”,
Thirteenth Conference on Hemoglobin Switching, Oxford, United Kingdom, September
2002

“Molecular control of β -globin gene switching”, Stowers Institute for Medical Research, Kansas
City, Missouri, November 2002

“Role of γ -globin gene silencing and chromatin sub-domains in globin gene switching”, *Annual
Meeting of the American Society of Hematology*, Philadelphia, Pennsylvania, December
2002

“Long-range regulation of globin gene expression by the locus control region”, University of
Kansas Medical Center, Kansas City, Kansas, January 2003

“Molecular control of human β -globin gene switching”, Vanderbilt University, Nashville,
Tennessee, February 2003

“Molecular control of human β -globin gene switching”, University of Louisiana at Lafayette,
Lafayette, Louisiana, February 2003

8. Honors

KUMC Faculty Research Award

9. Graduate, Medical, Postdoctoral, and Summer Students

Graduate students:

Kara Wagoner, Graduate rotation student

Susanna Harju, Ph.D. candidate

Anna Nunn, M.S. candidate

Postdoctoral Fellows:

Auste Geddes, Postdoctoral fellow

Rita Lee, Postdoctoral fellow

Summer students:

Maria Martinez, High school student
Taras Zelenchuk, High school student
Hanluen Kao, Undergraduate college student

10. Research Associates, Assistants, Technicians and Aides

Halyna Fedosyuk, Research Associate
Renee Neades, Research Associate
Lesya Zelenchuk, Research Assistant
Adrian Zelenchuk, Research Associate

Margaret G. Petroff

(September 1, 2002 through August 31, 2003)

Research Assistant Professor
Department of Anatomy and Cell Biology
University of Kansas Medical Center
Kansas City, KS 66160
Phone: 913 588-7030
Fax: 913 588-7180
Email: mpetroff@kumc.edu

1. Research Interests

Our research explores cross-talk between the reproductive and immune systems, with a current focus on the immunological functions of the placenta. We are currently investigating how the placenta actively mediates escape of the allogeneic fetus from rejection by the maternal immune system through production of immunomodulatory cell-associated and soluble molecules.

2. Publications (2002-2003)

a. published

Petroff M.G., Sedlmayr P., Azzola D., Hunt J.S. (2002) Decidual macrophages are potential targets for Class Ib HLA Molecules. *J. Reprod. Immunol.* 56, 3-17

Petroff M.G., Chen L., Phillips T.A., Hunt J.S. (2002) B7 family molecules: novel immunomodulators at the maternal-fetal interface. *Placenta* (Suppl. A) S95-S101

Petroff M.G., Chen L., Morgan K.A., Philips T.A., Sedlmayr P., Hunt J.S. (2003) B7 family molecules are favorably positioned at the human maternal fetal interface. *Biol. Reprod* 68, 1496-1504

Cannon M.J., **Petroff M.G.**, Pate J.L. (2003) Effects of prostaglandin F_{2a} and progesterone on the ability of bovine luteal cells to stimulate T lymphocyte proliferation. *Biol. Reprod.* 69, 695-700

Holtz R., Choi J., **Petroff M.G.**, Hunt J.S., Piskurich J., Murphy S.P. (2003) Class II Transactivator (CIITA) promoter methylation does not correlate with silencing of CIITA transcription in trophoblasts. *Biol. Reprod* 69, 915-924

b. in press

Hunt J.S., **Petroff M.G.** (2003) Placental immunology. *Encyclopedia of Hormones*, in press.

Petroff M.G., Hunt J.S. Immunity at the maternal-fetal interface. *Mucosal Immunology*, In Press.

c. abstracts

Petroff M.G. (2003) B7-H1 and B7-H2 expression and regulation in human placental trophoblast cells. 90th meeting of the American Association of Immunologists, Denver, Colorado.

3. Grant Support

National Institutes of Health, “Soluble HLA-G Isoforms and Immunomodulation”, F32 HD08660, Principal Investigator Margaret Petroff, \$32,500 (direct costs/year), Total duration of the award: March 1, 2000 through February 1, 2002.

KUMC, Lied Endowed Basic Science Pilot Research, “Immunoregulatory Functions of Trophoblast B7 Family Molecules”, Principal Investigator Margaret Petroff, \$35,000 (direct costs/year), Total duration of the award: February 1, 2002 through February 28, 2004.

Kansas City Area Life Sciences Institution, “Alterations of Proinflammatory Genes in Preeclampsia”, Principal Investigator Margaret Petroff, \$22,727 (direct costs/year), Total duration of the award: November 1, 2002 through April 3, 2004.

National Institute of Health, “Immunomodulatory B7 Family Proteins in the Placenta”, R01 HD045611, Principal Investigator Margaret Petroff, amount per year to be determined, Total duration of the award: January 1, 2004 through December 31, 2009.

4. Meetings Attended

Annual Meeting of the Society for the Study of Reproduction, August 2002, Baltimore, Maryland

Annual Meeting of the American Association of Immunologists, Denver, Colorado

Annual Meeting of the Society for the Study of Reproduction, August 2003, Cincinnati, Ohio

5. Journals Refereed

Ad Hoc Reviewer for:

<i>Biology of Reproduction</i>
<i>Fertility and Sterility</i>
<i>Journal of Immunology</i>
<i>Journal of Reproductive Immunology</i>
<i>Molecular Human Reproduction</i>
<i>Placenta</i>

6. Seminars presented

“B7 Proteins: Fetal Modulators of the Maternal Immune System” *Frontiers in Reproduction Fifth Annual Symposium: Immune Mechanisms in Pregnancy*. Cambridge, Massachusetts, June 2002.

“*The Immunology of Pregnancy: We All Escaped Mother’s Immune System, But How?*” Emporia State University, Emporia, Kansas, March 2003.

7. Honors

American Association of Immunologists, *Junior Faculty Travel Award*

8. Graduate, Medical, Postdoctoral, and Summer Students

Summer Students:

Hilary Rainbolt (Summer 2003)

Michael J. Soares

(September 1, 2002 through August 31, 2003)

Director of the Institute of Maternal-Fetal Biology
Professor of Molecular & Integrative Physiology
Professor of Obstetrics & Gynecology
University of Kansas Medical Center
Kansas City, KS 66160
Phone: 913 588-5691
Fax: 913 588-8287
Email: msoares@kumc.edu

1. Research Interests

Our laboratory is interested in molecular mechanisms and signaling events involved in the establishment and maintenance of pregnancy; including investigations on the prolactin gene family, intrauterine inflammatory and immune cells, uterine vasculature, and signaling pathways controlling the growth and differentiation of decidual and trophoblast cells.

2. Publications (2002-2003)

a. published

Ain, R., Müller, H., Sahgal, N., Dai, G., and **Soares, M.J.** (2002) Uteroplacental prolactin family: immunological regulators of viviparity. *Neuroimmune Biology* 2, 187-202

Audus, K.L., **Soares, M.J.**, and Hunt, J.S. (2002) Characteristics of the fetal/maternal interface with potential usefulness in the development of future immunological and pharmacological strategies. *Journal of Pharmacology and Experimental Therapeutics* 301, 402-409

Ain, R., Tash, J.S., and **Soares, M.J.** (2002) A simple method for the in situ detection of eosinophils. *Journal of Immunological Methods* 260, 273-278

Kamei, T., Jones, S.R., Chapman, B.M., McGonigle, K., Dai, G., and **Soares, M.J.** (2002) Activation and involvement of the phosphatidylinositol 3-kinase/akt-signaling pathway in the endocrine differentiation of trophoblast cells. *Molecular Endocrinology* 16, 1469-1481

Dai, G., Lu, L., Tang, S., Peal, M.J., and **Soares, M.J.** (2002) The prolactin family miniarray: a tool for evaluating uteroplacental/trophoblast endocrine cell phenotypes. *Reproduction* 124, 755-765

Wiemers, D.O., Shao, L.-J., Ain, R., Dai, G., and **Soares, M.J.** (2003) The mouse prolactin gene family locus. *Endocrinology* 144, 313-325

Ain, R., Tash, J.S., and **Soares, M.J.** (2003) Prolactin-like protein-A is a functional modulator of natural killer cells at the maternal-fetal interface. *Molecular and Cellular Endocrinology* 204, 65-74

Ain, R., Canham, L.N., and **Soares, M.J.** (2003) Gestational stage-dependent intrauterine trophoblast cell invasion in the rat and mouse: novel endocrine phenotype and regulation. *Developmental Biology* 260, 176-190

Wiemers, D.O., Ain R, Ohboshi, S., and **Soares, M.J.** (2003) Migratory trophoblast cells express a newly identified member of the prolactin gene family. *Journal of Endocrinology*, 179, 335-345.

Zhou, F., Tanaka, K., **Soares, M.J.**, and Yan, G. (2003) Characterization of an organic anion transport system in a placental cell line. *American Journal of Physiology*, 285, E1103-E1109.

b. abstracts

Takahashi, T., Lu, L., Ain, R., Alt, A., Li, C., Dai, G., Hashizume, K., Schuler, L.A., and **Soares, M.J.** (2002) A strategy for identifying bovine prolactin family interactions with target tissues. 35th Annual Meeting of the Society for the Study of Reproduction, Baltimore, Maryland

Dai, G., Peal, M.J., and **Soares, M.J.** (2002) Hepatomegaly and hepatic gene expression during pregnancy in the mouse. 35th Annual Meeting of the Society for the Study of Reproduction, Baltimore, Maryland

Alt, A., Dai, G., Peal, M.J., Ain, R., and **Soares, M.J.** (2002) Pregnancy-dependent splenomegaly and splenic gene expression. 35th Annual Meeting of the Society for the Study of Reproduction, Baltimore, Maryland

Ain, R., Dai, G., and **Soares, M.J.** (2002) Trophoblast cells invading the uterine mesometrial triangle possess a novel endocrine phenotype. 35th Annual Meeting of the Society for the Study of Reproduction, Baltimore, Maryland

Sahgal, N., Canham, L.N., and **Soares, M.J.** (2003) Fetal regulation of trophoblast cell invasion into the maternal uterine mesometrial vascular compartment. Annual Meeting of the Society for Pediatric Research, Seattle, Washington

3. Grant Support

National Institutes of Health, "Pregnancy-specific Modulation of Natural Killer Cells", HD37123, Principal Investigator, **Michael J. Soares**, \$168,348/year (direct costs/year), Total duration of the award: August 1, 1999 through July 30, 2002.

Mellon Foundation, "Maternal Adaptations to Implantation", Principal Investigators, **Michael J. Soares** and Guoli Dai, \$140,000/year (direct costs/year), Total duration of the award: April 1, 2000 through March 31, 2003.

National Institutes of Health, "Biology at the Maternal-Fetal Interface", HD39878, Principal Investigator, **Michael J. Soares**, \$583,391 (direct costs/year), Total duration of the award: May 1, 2002 through April 30, 2007.

National Institutes of Health, "Trophoblast Differentiation", HD20676, Principal Investigator, **Michael J. Soares**, \$202,500 (direct costs/year), Total duration of the award: May 1, 2002 through April 30, 2007.

National Institutes of Health, "Trophoblast Differentiation-Supplement for Dr. Juan Jose Bustamante", HD20676S, Principal Investigator, **Michael J. Soares**, \$46,000 (direct costs/year), Total duration of the award: May 1, 2002 through April 30, 2007.

National Institutes of Health, "Trophoblast Differentiation-Supplement for Human Embryonic Stem Cell Research, RO1-HD20676-S2, Principal Investigator, **Michael J. Soares**, \$75,000 (direct costs/year), Total duration of the award: May 1, 2003 through April 30, 2005.

Hall Family Foundation, "Hypoxia and Vascular Programming", Principal Investigator, **Michael J. Soares**, \$75,000 (direct costs/year), Total duration of the award: July 1, 2003 through June 30th, 2005.

National Institutes of Health, "Fetal Regulation of the Placenta", KO8 HD42171, Principal Investigator, Namita Sahgal, \$120,000 (direct costs/year), total duration of the award: April 1, 2002 through March 31, 2007 [**Mentor: Michael J. Soares**].

National Institutes of Health, "Trophoblast Invasion", F31 HD045052, National Research Service Award Predoctoral Fellowship, Principal Investigator, Jennifer Ho-Chen, \$28,000 (direct costs/year), Total Duration of the award: June 2003 through May 2007 [**Mentor: Michael J. Soares**].

4. Meetings Attended

Annual Meeting of the Society for the Study of Reproduction, August 2002, Baltimore, Maryland

International Conference on the Female Reproductive Tract, June 2003, Frauenchiemsee, Germany

NIDA Sponsored Workshop on Placental Proteins, Drug Transport, and Fetal and Perinatal Development", Bethesda, Maryland, August 2003

5. Journals Refereed

Senior Editor, *Journal of Endocrinology*

Ad Hoc Reviewer for:

<i>Journal of Endocrinology</i>
<i>Endocrinology</i>
<i>Journal of Clinical Endocrinology and Metabolism</i>

<i>Molecular and Cellular Biology</i>
<i>Molecular Endocrinology</i>
<i>Developmental Dynamics</i>
<i>Mammalian Genome</i>
<i>Pediatric Research</i>
<i>Biology of Reproduction</i>
<i>Endocrine</i>
<i>Molecular and Cellular Endocrinology</i>
<i>Placenta</i>

6. Grants Reviewed, Consultation

Americas Fellowship Program

Consultant for the Perinatal Research Center, Department of Pediatrics, University of Colorado Health Sciences Center, Aurora, CO, on a research project entitled: “Fetoplacental amino acid metabolism in IUGR pregnancies”, 2002-2007

Organizer of an American Physiological Society sponsored symposium entitled: "The Maternal-Fetal Dialogue", Washington, D.C., April 17-21, 2004

7. Seminars Presented

“The prolactin family and pregnancy”, Children’s Mercy Hospital, Kansas City, Missouri, November 2002

“Biology at the maternal-fetal interface: the prolactin gene family expansion”, Department of Physiology, Wright State University, Ohio, November 2002

“The prolactin family expansion and pregnancy”, Reproductive Biology Program, University of Kentucky, Lexington, Kentucky, May 2003

“The prolactin family and pregnancy”, *International Conference on the Female Reproductive Tract*, Frauenchiemsee, Germany, June 2003

“Maternal-fetal interface, trophoblast invasion, and pregnancy-specific cytokines”, *NIDA Sponsored Workshop on Placental Proteins, Drug Transport, and Fetal and Perinatal Development*”, Bethesda, Maryland, August 2003

8. Graduate, Medical, Postdoctoral, and Summer Students

Graduate Students:

Jennifer Ho-Chen (2002-present) Recipient of an NIH NRSA Predoctoral Fellowship

Postdoctoral Fellows:

Dr. Rupasri Ain (1999-present); Recipient of a University of Kansas Medical Center Training Program in Biomedical Sciences Fellowship and a Postdoctoral Fellowship from the American Heart Association.

Dr. Toru Takahashi (2001-2003)

Dr. Shigeki Oboshi (2002-present)

Dr. Juan J. Bustamante (2002-present)

Dr. S.M. Khorshed Alam (2003-present)

Dr. Toshihiro Konno (2003-present)

Dr. Juan A. Arroyo (2003-present)

Summer Students:

My-Linh Trinh (Summer 2001-Summer 2003)

9. Research Associates, Assistants, Technicians and Aides

Lindsey Kent, Research Assistant (2001-present)

Adam Alt, Research Assistant (2001-present)

Stacy McClure, Administrative Assistant (2002-present)

William E. Truog

(September 1, 2002 through August 31, 2003)

Sosland Family Endowed Chair in Neonatal Research
Children's Mercy Hospitals and Clinics
Professor of Pediatrics
Section of Neonatal-Perinatal Medicine
Director, Neonatal-Perinatal Medicine Fellowship Program
University of Missouri-Kansas City School of Medicine
2401 Gillham Road
Kansas City, MO 64108
Adjunct Professor of Molecular and Integrative Physiology
University of Kansas School of Medicine
Kansas City, KS 66160
Phone: 816-234-3592
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1. Research Interests

The long term goal of Dr. Truog and other investigators in the Pulmonary Developmental Biology Research Laboratories of Children's Mercy Hospitals and Clinics at the University of Missouri - Kansas City School of Medicine is to improve understanding of how the lungs of newborn infants are injured, and to investigate new therapies for pulmonary disorders. One specific goal of the laboratory is to assess both beneficial and toxic effects of the potent therapeutic agent, inhaled nitric oxide, both at the bedside and in the laboratory. Our group has focused on studying potential toxicity of combined exposure to oxygen and to nitric oxide in neonatal piglets. We seek to learn about alterations in structural elements of the lung, as well as altered molecular expression and protein production of growth factors in the lung. Our parallel studies in humans have examined the impact of profoundly preterm delivery and its consequences. We have studied pulmonary microvascular development, assessing quantitatively by light and electron microscopy the state of the pulmonary microvasculature following exposure to oxygen and assisted ventilation.

Other studies undertaken in our laboratory include assessment, both in humans and in animals, of lipid and peptide mediators of pulmonary vascular reactivity and the effects of various pulmonary disorders on the metabolism of these vasoactive substances in the developing lung. Investigations in our laboratory also include the assessment of different patterns of lung inflation as provided by assisted breathing devices and their relative contributions to lung injury in immature lungs.

2. Publications (2002-2003)

a. published

Ekekezie, I.I., Thibeault, D.W., **Truog, W.E.** (2003) Endostatin and vascular endothelial cell growth factor (VEGF) in piglet lungs; effect of inhaled nitric oxide and hyperoxia, *Pediatr Res*. 53(3), 440-446

Thibeault, D.W., Mabry, S.M., Ekekezie, I.I., Zhang, X., **Truog, W.E.** (2003) Collagen scaffolding during development and its deformation with chronic lung disease. *Pediatrics*. 111(4), 766-776

Truog, W.E., Pallotto, E., Clark, P., Banks, B., Kaftan, H.A., Ekekezie, I.I., Norberg, M., Ballard, R.A. (2002) Interaction of endogenous endothelin-1 and inhaled nitric oxide in term and preterm infants. *Clin Sci (Lond)*, 103 Suppl 48, 294S-297S

Kaftan, H.A., Clark, P.L., Norberg, M., Garg, U., Thibeault, DW., **Truog, W.E.** (2003) Endogenous production of nitric oxide in endotoxemic piglets. *Biol Neonate* 83, 42-48

Truog, W.E., Castor, C.A., Sheffield, M.J. (2003) Neonatal nitric oxide use: predictors of response and financial implications. *J Perinatol* 23, 128-132

Truog, W.E. (2003) Genomic and complex neonatal disorders: maybe we're getting somewhere. *J Perinatol* 23, 91-93

Ballard, P.L., Merrill, J.D., Godinez, R.I., Godinez, M.H., **Truog, W.E.**, Ballard, R.A. (2003) Surfactant protein profile of pulmonary surfactant in premature infants. *Am J Respir Crit Care Med* 168, 1123-1128

b. in press

Thibeault, D.W., **Truog, W.E.**, Ekekezie, I.I. (2003) Acinar arterial changes with chronic lung disease of prematurity in the surfactant era. *Pediatr Pulm.*, in press

Olsen, S.L., Clark, P.L., Thibeault, D.W., Norberg, M., **Truog, W.E.** (2003) Exhaled nitric oxide and tracheal endothelin-1 in preterm infants with and without RDS. *Pediatr Pulm.*, in press

Ekekezie, I.I., Thibeault, D.W., Simon, S.D., Norberg, M., Merrill, J., Ballard, R., Ballard, P., **Truog, W.E.** (2003) Low levels of tissue inhibitors of metalloproteinases with a high MMP-9/TIMP-1 ratio are present in the tracheal aspirate fluids of infants developing CLD. Provisionally accepted for publication, *Pediatrics*

c. abstracts

Truog W.E., Ekekezie, I.I., Xu, D. (2003) Gene expression and chronic lung disease: directed microarray analysis. NHLBI Symposium "From Genome to Disease: A Symposium of High Throughput Biology," NIH, Bethesda, Maryland (Poster presentation)

Ehlert, C.A., Thibeault, D.W., Ekekezie, I.I., Mabry, S., Rezaiekhalthigh, M., Zhang, X., Molteni, A., **Truog, W.E.** (2003) The response to the immature rat in intra-tracheal bleomycin as a model for pulmonary fibrosis. *Pediatr Res* 53(4), 429A (Poster presentation)

Sheffield, M.J., Thibeault, D.W., Mabry, S., **Truog, W.E.** (2003) Human pulmonary nitric oxide synthases: Normal development and effects of chronic lung disease. *Pediatr Res* 53(4), 411A (Poster)

Ehlert, C.A., Thibeault, D.W., Ekekezie, I.I., Mabry, S., Rezaiekhalthigh, M., Zhang, X., Molteni, A., **Truog, W.E.** (2003) The response of the immature rat to intratracheal bleomycin as a model for pulmonary fibrosis. *Pediatr Res* 53(4), 429A (Poster)

Truog, W.E., Jackson, J.K., Braun, W.J., Kilbride, H.W. (2003) Early postnatal emergent nitric oxide use in hypoxemic very preterm infants: Reason for optimism? *Pediatr Res* 53(4), 510A

d. books, book chapters published

Truog, W.E. (2003) Pulmonary Hypoplasia With and Without Congenital Diaphragmatic Hernia. In: *Rudolph's Textbook of Pediatrics, 21st ed.* WB Saunders, Philadelphia, PN

Truog, W.E. (2003) Pulmonary Gas Exchange in the Developing Lung. In: R. Polin and W. Fox, eds. *Fetal and Neonatal Physiology, 3rd ed.* W.B. Saunders Co., Philadelphia, PA, in press

3. Grant Support

“Inflammation, Matrix Disruption and Chronic Lung Disease”, K23 HD01316 NIH/NHLBI, Principal Investigator, **William E. Truog**, \$663,000 (total cost), Total duration of the award: September 1, 1999 through August 31, 2004.

“Low Dose Inhaled Nitric Oxide for Chronic Lung Disease in the Premature Infant”, U01 HL 62514 NIH/NHLBI Co-PI, Site: Principal Investigator, **William E. Truog**, \$800,000 (total cost), Total duration of the award: March 1, 2000 through March 1, 2005.

“Lung Inflammation, TLRs and Immaturity”, R01 HL 70560-01 NIH, Principal Investigator, **William E. Truog**, \$915,000 (total cost), Total duration of the award: March 1, 2001 through February 29, 2006.

“Pathogenesis and Therapy for Hyperoxic Lung Injury”, Hall Family Foundation Research Grant, Co-Principal Investigator, **William E. Truog**, \$100,000 (total cost), Total duration of the award: November 2001 through October 31, 2003.

Physician Scientist Award, Children’s Mercy Hospitals and Clinics, Principal Investigator, **William E. Truog**, \$500,000, Total duration of the award: (ongoing).

Sosland Family Endowed Chair in Neonatology Research, Principal Investigator, **William E. Truog**, \$1.2 million, Total duration of the award: 2001 and on.

Hall Family Foundation, "Hypoxia and Vascular Programming", Principal Investigator, Michael J. Soares, \$75,000 (direct costs/year), Total duration of the award: July 1, 2003 through June 30th, 2005 [Co-Principal Investigator, Subproject II: William E. Truog].

4. Meetings Attended

NHLBI Symposium “From Genome to Disease: A Symposium of High Throughput Biology,” July 2003, NIH, Bethesda, Maryland.

5. Journals Refereed

Ad hoc reviewer for:

<i>American Journal of Respiratory and Critical Care Medicine</i>
<i>Archives of Disease in Childhood</i>
<i>Biology of the Neonate</i>
<i>Journal of Applied Physiology</i>
<i>Pediatrics</i>
<i>Pediatric Pulmonology</i>
<i>Pediatric Research</i>

6. Committees, Consulting, etc.: National

Member Special Emphasis Review Panel, NHLBI (2003)

2000-2003 Elected Chairman of Organization of Neonatal-Perinatal Training Program Directors (ONTPD) Council

7. Seminars Presented

“Nitric Oxide and ELBW Infants: Few Facts, Some Hope, Lost of Speculation”, Pacific Northwest Neonatal Symposium, Seattle, Washington, 2003

“Genetics and Nitric Oxide Therapy” Hot Topics in Neonatology, Washington, DC 2003

“Hyperoxia, Nitric Oxide and Pulmonary Injury in the Developing Lung”, Kansas City Area Life Sciences Initiative, Kansas City, Missouri 2003

8. Graduate, Medical, Postdoctoral Fellows, and Summer Students

Postdoctoral Fellows:

Carey Ehlert, M.D. (1999-2003)

Susannah P. Ford, M.D. (2001-present)

Mark J. Sheffield, M.D. (2001-present)

David W. Minderman, M.D. (2002-present)

Emily McNellis, M.D. (2003-present)

9. Research Associates, Assistants, Technicians and Aides

Dong Xu, M.D. (2002-present)

Carey Ehlert, M.D. (2003-present)

Susannah P. Ford, M.D. (2001-present)
Mark J. Sheffield, M.D. (2001-present)
David W. Minderman, M.D. (2002-present)
Emily McNellis, M.D. (2003-present)
Sherry Mabry (1990-present)
Mike Norberg (1993-present)
Mo Rezaiekhalthigh (1990-present)

Michael W. Wolfe

(September 1, 2002 through August 31, 2003)

Dept. of Molecular & Integrative Physiology
University of Kansas Medical Center
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1. Research Interests

Expression of luteinizing hormone (LH) in pituitary gonadotropes and chorionic gonadotropin (CG) in placenta are essential to mammalian reproduction. These hormones are composed of two subunits - a common alpha-subunit and distinct beta-subunits. Research in my laboratory is directed towards understanding the cellular and molecular mechanisms involved in tissue-specific and hormonal regulation of the genes encoding these hormones. This involves studying the mechanisms regulating cell differentiation, elucidation of transcription factors regulating basal expression, and identifying the signal transduction pathways and associated transcription factors used by extracellular factors (hormones, growth factors, cytokines) to regulate gene expression. A variety of methodological approaches are utilized in these investigations including in vitro DNA-protein binding assays, cell culture and transient transfections, assays evaluating gene transcription and protein expression, and the use of transgenic mice.

2. Publications (2002-2003)

a. published

Call, G.B., and **Wolfe, M.W.** (2002) Species differences in GnRH activation of the LH β promoter: role of Egr1 and Sp1. *Mol. Cell. Endocrinol.* 189, 85

Thway, T.M., and **Wolfe, M.W.** (2002) An activator protein-1 complex mediates epidermal growth factor regulation of equine glycoprotein α -subunit expression in trophoblast cells. *Biol. Reprod.* 67, 972

b. abstracts

Wolfe, M.W., Roberson, M.S. and Call, G.B. (2002) Functional differences in the GnRH signal transduction pathways between α T3-1 and L β T2 cells. 35th Annual Meeting of the Society for the Study of Reproduction, Baltimore, Maryland

Canham, L.N., Sahgal, N., **Wolfe, M.W.** and Soares, M.J. (2003) Selective involvement of the phosphatidylinositol 3-kinase/AKT signaling pathway in the regulation of trophoblast cell

differentiation. 36th Annual Meeting of the Society for the Study of Reproduction, Cincinnati, Ohio

Jablonka-Shariff, A., Gerber, B., Daphna-Iken, D., Bousfield, G.R., **Wolfe, M.W.**, Roser, J.F., and Boime, I. (2003) Expression of the equine LH β /CG β and α subunits from transfected CHO cells: Comparison with the human LH β and CG β subunits. 36th Annual Meeting of the Society for the Study of Reproduction, Cincinnati, Ohio

3. Grant Support

National Institutes of Health, "Cytokine regulation of trophoblast function", (RO3) HD39695, Principle Investigator: Michael W. Wolfe, \$ 50,000(direct cost/year), Total duration of the award: June 1, 2001 through May 31, 2003 (1 yr no cost extension).

KUMC Research Institute (Lied), "Nab regulation of Egr function", Principle Investigator: Michael W. Wolfe, \$50,000 (direct cost/year), Total duration of the award: March 1, 2002 through February 28, 2003 (1 yr no cost extension).

National Institutes of Health, "Trophoblast Differentiation", HD20676, Principal Investigator, Michael J. Soares, \$202,500 (direct costs/year), Total duration of the award: May 1, 2002 through April 30, 2007 [Co-Investigator: Michael W. Wolfe].

National Institutes of Health, "Trophoblast Differentiation-Supplement for Human Embryonic Stem Cell Research, RO1-HD20676-S2, Principal Investigator, Michael J. Soares, \$75,000 (direct costs/year), Total duration of the award: May 1, 2003 through April 30, 2005 [Co-Investigator: Michael W. Wolfe].

4. Meetings Attended

35th Annual Meeting of the Society for the Study of Reproduction, August 2002, Baltimore, Maryland.

5. Journals Refereed

Ad Hoc Reviewer for:

<i>Endocrinology</i>
<i>Biology of Reproduction</i>
<i>Journal of Biological Chemistry</i>
<i>Molecular Endocrinology</i>
<i>Journal of Molecular Endocrinology</i>
<i>American Journal of Physiology</i>

6. Committees, Consulting, etc.: National

USDA Competitive Research Grants Program

National Institutes of Health - HED1 grant review, 2002

Kansas City Area Life Sciences Institute, Inc. – Grant review in 2003

7. Seminars Presented

“Regulation and function of Egr1 in pituitary gonadotropes”, Department of Pharmacology, KUMC, January 2003

“Regulation and function of Egr1 in pituitary gonadotropes”, Department of Animal Sciences, Kansas State University, Manhattan, Kansas, May 2003

8. Graduate, Medical, Postdoctoral, and Summer Students

Graduate Students:

Jennifer Ho-Chen (Spring 2003) Recipient of an NIH NRSA Predoctoral Fellowship

Summer Students:

Christina Conrad (Summer 2003)

9. Research Associates, Assistants, Technicians and Aides

Patricia Wolfe, Technician



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