

# **Appendix 1**

## **Adult Stem Cell Investigator Information**

## **Adult Stem Cell Investigators**

Robert Bacallao, Nephrology  
Hal Broxmeyer, Walther Oncology Center  
Edward Chan, Hematology/Oncology  
Rebecca Chan, Pediatrics/Neonatology  
Cheong-Hee Chang, Microbiology/Immunology  
Tien-Min Chu, Biomedical Engineering  
Kristin Chun, Biochemistry/Molecular Biology  
Kenneth Cornetta, Medical and Molecular Genetics  
Alexander Dent, Microbiology/Immunology  
Loren Field, Cardiology  
Shao-Ling Fong, Biochemistry/Molecular Biology  
William Goebel, Hematology/Oncology  
Laura Haneline, Pediatrics/Neonatology  
Eri Hashino, Otolaryngology/Head and Neck Surgery  
Paul Haut, Pediatric Transplantation  
Soon-Cheol Hong, Microbiology/Immunology  
Dongming Hou, Vascular Biology and Medicine  
David Ingram, Pediatrics/Neonatology  
Reuben Kapur, Neonatology  
Patrick Loehrer, Hematology/Oncology  
Linda Malkas, Hematology/Oncology  
Keith March, Cardiology/Vascular Biology  
Harikrishna Nakshatri, Surgery  
Christie Orschell, Hematology/Oncology  
Louis Pelus, Microbiology and Immunology  
Karen Pollok, Pediatrics  
Jalees Rehman, Cardiology  
Joseph Ruiz, Pediatrics  
Edward Srour, Pediatrics  
David Stocum, Regenerative Medicine  
Michael Sturek, Cellular Physiology  
David Wilkes, Pulmonary  
Stephen Williams, Cancer Center  
Mervin Yoder, Pediatrics/Neonatology

## BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Hal E. Broxmeyer, Ph.D.	POSITION TITLE Distinguished Professor, Chairman, and Scientific Director		
eRA COMMONS USER NAME HBROXMEY			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Brooklyn College, City University of New York	B.Sc.	1966	Biology
Long Island University, Brooklyn, New York	M.S.	1969	Microbiology
New York University, New York, New York	Ph.D.	1973	Exptl. Hematology
Queens University, Department of Medicine, Kingston, Ontario	Postdoc	1973-75	Exptl. Hematology

### Positions Held (awards underlined):

11/1/76 – 5/78 Research Associate, Sloan-Kettering Institute, N.Y.; Special Fellow, Leukemia Society of America, July 1976-June 1978; Mellor Award 76, 77.

6/1/78 – 1/31/83 Assistant Member (Associate), Sloan Kettering Institute, N.Y.; Scholar, Leukemia Society of America, 1978-83.

1/1/80 – 6/30/83 Assistant Professor of Biology, Sloan Kettering Division, Cornell University Graduate School of Medical Sciences, N.Y., Boyer Award, 1983.

2/1/83 – 6/30/83 Associate Member, Sloan-Kettering Institute, N.Y.

7/1/83 – 6/30/86 Associate Professor of Medicine, Microbiology and Immunology, Indiana University School of Medicine.

7/1/86 – 12/31/96 Mary Margaret Walther Professor of Medicine, Microbiology and Immunology, Indiana University School of Medicine; Merit Award, NCI 1987-1995.

2/1/88 - Present Scientific Director, Walther Oncology Center

1/1/97 - Present Chairman and Mary Margaret Walther Professor of Microbiology and Immunology, Professor of Medicine, Indiana University School of Medicine; World of Difference Award for Outstanding Achievements in Health Care, Indiana University Health Forum, 1997; Who's Who in Health Care Heroes Award, Indianapolis Business Journal, 2002; Karl Landsteiner Award, American Association of Blood Banks, 2002; Prestigious External Award Recognition, Indiana University Purdue University of Indianapolis, 2003; Distinguished Professor, 2004.

**Memberships (Partial Listing):** Review Committees: Present: Council Member and Chairman, Bd. Sci Counselors, Natl. Biomed. Space Res. Inst./NASA, 98-Present; Council, ASH, 02-05; Ad. Hoc., NCI Cancer Centers, NHLBI, NIDDK, DOD. Past: NIH Hem II Study Section 81-86, 95-June,00, chair: 97-June,00; Leuk. & Lymphoma Soc. Natl. Study Section, 89-95, 99-04; NHLBI Advisory Bd. 92-94; Ad. Hoc for ACS, NSF, VA, etc. Edit. Bds.: Present: J. Exp. Med.; Int. J. Hematol.; Annal Hematol.; Cell Transpl.; J. Lab. Clin. Med.; Stem Cells; Crit. Rev. Oncol/Hematol.; J. Leuk. Biol. (Editor); Brit. J. Haematol. (Editor); Biol. Bl. Marrow Transpl.; Cytokines, Cells, Mol. Therapy; Stem Cells and Development (Senior Editor); Faculty 1000 (Co-chair, Hematopoiesis). Past: Blood, J. Immunol., Exp. Hematol., Acta Haematol., Cell Therapy. Reviewer for over 20 journals this year. Societies: ASH (Council, Publication committee; Past Chair, Budget subcommittee), ISEH (Past President), AAI, AACR, Soc. Leuk. Biol.(former councilor), NYAS, AAAS, AFCR

### Publications (Selected from 431 Papers in Referred journals; 161 book chapters/reviews and 446 abstracts (Not included):

Kim, C.H., Hangoc, G., Cooper, S., Helgason, C.D., Yew, S., Humphries, R.K., Krystal, G., and Broxmeyer, H.E. 1999. Altered responsiveness to chemokines due to targeted disruption of SHIP. J. Clin. Invest. 104:1751-1759.

Youn, B.S., Kim, C.H., Smith, F.O. and Broxmeyer, H.E. 1999. TECK, an efficacious chemoattractant for human thymocytes, uses GPR-9-6/CCR9 as a specific receptor. Blood, 94:2533-2536.

Zhang, S., Fukuda, S., Lee, Y.-H., Hangoc, G., Cooper, S., Spolski, R., Leonard, W.J. and Broxmeyer, H.E. 2000. Essential role of signal transducer and activator of transcription (Stat)5a but not Stat5B for Flt3-dependent signaling. J. Exp. Med. 192:719-728.

Mantel, C., Braun, S.E., Lee, Y.H., Kim, Y.-J. and Broxmeyer, H.E. 2001. The interphase microtubule damage checkpoint defines an S-phase commitment point and does not require p21<sup>waf1</sup>. Blood. 97:1505-1507.

- Lee, Y.H., Mantel, C., Anzai, N., Braun, S.E. and Broxmeyer, H.E. 2001. Transcriptional and ERK1/2 dependent synergistic upregulation of p21<sup>cip1/waf1</sup> associated with steel factor synergy in MO7e. *Biochem Biophys Res Comm.* 280:675-683.
- Lee, Y.H., and Broxmeyer, H.E. 2001. Synergistic activation of RSK correlates with c-fos induction in MO7e cells stimulated with GM-CSF plus steel factor. *Biochem Biophys Res Comm.* 281:897-901.
- Youn, Byung-S., Kim, Young, Y.-J., Mantel, C. and Broxmeyer, H.E. 2001. Blocking of c-FLIP<sub>L</sub>-independent cycloheximide-induced apoptosis or Fas-mediated apoptosis by the CC chemokine receptor (CCR) 9/TECK interaction. *Blood.* 98:925-933.
- Anzai, N., Lee, Y.-H., Youn, B.S., Fukuda, S., Kim, Y.-J., Mantel, C., Akashi, M., and Broxmeyer, H.E. 2002. c-kit associated with the transmembrane 4 superfamily proteins constitutes a functionally distinct subunit in human hematopoietic progenitors. *Blood.* 99:4413-4421.
- Broxmeyer, H.E., Bruns, H., Zhang, S., Cooper, S., Hangoc, G., McKenzie, A.N.J., Dent, A., Schindler, U., Naeger, L.K., Hoey, T., and Kaplan, M.K. 2001. Th1 cells regulate hematopoietic progenitor cell homeostasis by production of oncostatin M. *Immunity.* 16:1-20.
- Kim, Y.J., Brutkiewicz, R.R., and Broxmeyer, H.E. 2002. Role of 41BB in the (CD137) functional activation of cord blood CD28-negative CD8<sup>+</sup> cells. *Blood.* 100:3253-3260.
- Lee, Y., Gotoh, A., Kwon, H.-J., You, M., Kohli, L., Mantel, C., Cooper, S., Hangoc, G., Miyazawa, K., Ohyashiki, K., and Broxmeyer, H.E. 2002. Enhancement of intracellular signaling associated with hematopoietic progenitor cell survival in response to SDF-1/CXCL12 in synergy with other cytokines. *Blood.* 99:4307-4317.
- Mantel, C.R., Gelfanov, V.M., Kim, Y.-J., McDaniel, A., Lee, Y.H., Boswell, H.S., and Broxmeyer, H.E. 2002. P21<sup>waf-1</sup>-Chk1 Pathway Monitors G1-Phase Microtubule Integrity and Is Crucial for Restriction Point Transition. *Cell Cycle.* 1:(5)327-336.
- Broxmeyer, H.E., Cooper, S., Kohli, L., Hangoc, G., Lee, Y.H., Mantel, C., Clapp, D.W., and Kim, C.H. 2003. Transgenic expression of stromal cell derived factor-1/CXCL12 enhances myeloid progenitor cell survival/anti-apoptosis in vitro in response to growth factor withdrawal and enhances myelopoiesis in vivo. *J Immunol.* 170:421-429.
- Christopherson, K.W., Hangoc, G., and Broxmeyer, H.E. 2002. Cell surface petidose CD26/DPPIV regulates CXCL12/SDF-1 $\alpha$  mediated chemotaxis of human CD34<sup>+</sup> progenitor cells. *J. Immunol.* 169:7000-7008.
- Broxmeyer, H.E., Srour, E.F., Hangoc, G., Cooper, S., Anderson, J.A., and Bodine, D. 2002. High efficiency recovery of hematopoietic progenitor cells with extensive proliferative and ex-vivo expansion activity and of hematopoietic stem cells with NOD/SCID mouse repopulation ability from human cord blood stored frozen for 15 years. *Proc Natl Acad Sci USA.* 100:645-650.
- Li, G., Kim, Y.-J., Mantel, C., and Broxmeyer, H.E. 2003. P-selectin enhances generation of CD14<sup>+</sup> CD16<sup>+</sup> dendritic-like cells and inhibits macrophage maturation from peripheral blood monocytes. *J. Immunol.* 171:669-677.
- Tao, W., Hangoc, G., Hawes, J.W., Si, Y., Cooper, S., and Broxmeyer, H.E. 2003. Profiling of differentially expressed apoptosis-related genes by cDNA arrays in human cord blood CD34<sup>+</sup> cells treated with VP-16 etoposide. *Exp. Hematol.* 31:251-260.
- Broxmeyer, H.E., Kohli, L., Kim, C.H., Lee, Y., Mantel, C., Cooper, S., Hangoc, G., Shaheen, M., Li, X., and Clapp, D.W. 2003. Stromal Cell Derived Factor-1/CXCL12 Enhances Survival/Anti-Apoptosis of Hematopoietic Stem and Myeloid Progenitor Cells: Direct Effects Mediated Through CXCR4 and G $\alpha$ i Proteins. *J. Leuk. Biol.* 75:630-638.
- Tao, W., Hangoc, G., Cooper, S., and Broxmeyer, H.E. 2003. SDF-1/CXCL12 enhances retroviral-mediated gene transfer into human and murine hematopoietic progenitor cells. *Gene Therapy.* 11:61-69.
- Christopherson, K.W. II, Hangoc, G., Mantel, C., and Broxmeyer, H.E. 2004. Enhancement of hematopoietic stem cell transplantation by CD26 inhibition/deletion. *Science.* 305:1000-1003.
- Tao, W., Wang, M., Voss, E.D., Cocklin, R.R., Smith, J., Cooper, S., and Broxmeyer, H.E. 2004. Comparative proteomic analysis of human CD34<sup>+</sup> stem/progenitor cells and mature CD15<sup>+</sup> myeloid cells. *Stem Cells.* 22:1003-1014.
- Broxmeyer, H.E., Clapp, D.W., Orschell, C.M., Hangoc, G., Cooper, S., Plett, A., Liles, W.C., Li, X., Graham-Evans, B., Calandra, G., Bridger, G., Dale, D.C., and Srour, E.F. 2005. Rapid mobilization of murine and human stem and progenitor cells with AMD3100, a CXCR4 antagonist. *J Exp Med.* 201:1307-1318.
- Kim, Y.-J., Stringfield, T.M., Chen, Y., and Broxmeyer, H.E. 2005. Modulation of cord blood CD8<sup>+</sup> T-cell effector differentiation by TGF- $\beta$ 1 and 4-1BB costimulation. *Blood.* 105:274-281.
- Yu, R. Y.-L., Wang, X., Pixley, F.J., Yu, J.J., Dent, A.L., Broxmeyer, H.E., Stanley, E.R., and Ye, B.H. 2005. BCL-6 negatively regulates macrophage proliferation by suppressing IL-6 production. *Blood.* 105:1777-1784.
- Basu, S., and Broxmeyer, H.E. 2005. Transforming growth factor- $\beta$ 1 modulates responses of CD34<sup>+</sup> cord blood cells to stromal cell derived factor-1/CXCL12. *Blood.* 106:485-493.
- Li, G., Kim, Y.J., and Broxmeyer, H.E. 2005. Macrophage colony-stimulating factor drives cord blood monocyte differentiation into IL-10<sup>high</sup>IL-12<sup>absent</sup> dendritic cells with tolerogenic potential. *J. Immunol.* 174:4706-4717.

### Research Projects Ongoing or Completed During the Last 3 Years:

**"Mechanisms of Synergistic Regulation of Stem/Progenitors"**

Principal Investigator: Hal E. Broxmeyer, Ph.D.

Agency: NHLBI.

Type: RO1(HL56416) Dr. Broxmeyer has had this grant for over 25 years under several other names in which an RO1 and MERIT award were merged. Current Period: 4/1/05-3/31/09.

The aims are: to evaluate effects of IL-20 and SCF on proliferation of hematopoietic stem (HSC) and progenitor (HPC) cells, and self-renewal of HSC and to determine mechanisms of action and roles of intracellular signaling in these effects.

**"Chemokines/Cytokines and Receptors in Stem Cell Homing"**

Principal Investigator: Hal E. Broxmeyer, Ph.D.

Agency: NIDDK.

Type: RO1(DK53674) - Period: 9/1/97 – 1/31/06

The aim is to study the hypothesis that regulation of migration, homing and mobilization involves a combination of cytokine/cytokine receptor directed effects and that members of the chemokine family of cytokines and their receptors are intimately involved in modulation of these events.

Minority Supplement to DK53674; Period: 09/1/03 – 01/31/06.

**"Cytokine Enhancement of Myeloid Progenitor Cell Survival"**

Principal Investigator: Hal E. Broxmeyer, Ph.D.

Agency: NHBLI

Type: RO1 (HL67384-01) – Period 6/15/01 – 5/30/05. (This grant was submitted for competitive renewal, received a 28%% and will need to be revised. A no-cost extension has been applied for.)

The aims are to determine cellular and intracellular effects of SDF-1, Flt3-L, and TPO alone and in combination on prolonging the survival of myeloid progenitor cells.

A supplement to HL67384 on studying Human Embryonic Stem Cells; Period: 06/15/03 – 05/31/05.

**"Regulation of Hematopoietic and Tumor Cell Production"**

Principal Investigator: Hal E. Broxmeyer, Ph.D.

Agency: NIDDK.

Type: T32(DK07519) - Period: 7/1/85 – 6/30/05. (Competitive renewal received a 140 priority score and will be funded in fiscal year 2006 for years 21-25.)

This is a training program for graduate students and for PhD, MD/PhD, and MD post-docs.

**"Bridges to the Doctorate"**

Principal Investigator: Hal E. Broxmeyer, Ph.D.

Agency: GM

Type: R25(GMO67592) – Period 1/1/03 – 12/31/06.

This is a training program for graduate training for minority students for the M.S. degree at Jackson State; Mississippi to help train their students and faculty to enhance the possibility that the students will pursue a Ph.D. degree when they finish their Master's degree at Jackson State. The competitive renewal received a 161 priority score and will be funded.

**"Basic Science Studies on Gene Therapy of Blood Diseases"**

Principal Investigator: Hal E. Broxmeyer, Ph.D.

Agency: NHLBI

Type: T32 HL07910 – Period 7/1/04 – 6/30/09

This trains PhD, MD, MD/PhD and graduate students in the area of gene transfer and gene therapy.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Edward M. Chan, M.D.		POSITION TITLE Assistant Professor of Medicine	
eRA COMMONS USER NAME			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Stanford University, Stanford, CA	B.S., Honors	1988	Biological Sciences
Indiana University, Indianapolis, IN	M.D.	1992	Medicine

**A. Positions and Honors****Positions and Employment**

1992-1995 Resident in Internal Medicine, Indiana University Medical Center, Indianapolis, IN  
 1995-1998 Fellow in Hematology-Oncology, UCLA Medical Center, Los Angeles, CA  
 1998-2002 Lecturer of Medicine, Indiana University School of Medicine, Indianapolis, IN  
 2002-present Assistant Professor of Medicine, Indiana University School of Medicine, Indianapolis, IN

**Other Experience and Professional Memberships**

1992-present Sigma Xi, The Scientific Research Society  
 1992-present American Medical Association  
 1992-present American College of Physicians  
 1993-present American Association for the Advancement of Science  
 1993-present Diplomate of the National Board of Medical Examiners  
 1995-present Physician and Surgeon, Medical Board of California  
 1995-present Physician, Medical Licensing Board of Indiana  
 1995-present Diplomate in Internal Medicine, American Board of Internal Medicine  
 1998-present American Association for Cancer Research  
 1999-present Diplomate in Medical Oncology, American Board of Internal Medicine  
 2002-present American Society of Hematology

**Honors**

1983 Cum Laude Society  
 1983 Harvard Prize Book  
 1983 Brown University Book Award  
 1984 Valedictorian/Scholarship Award, The Head-Royce School  
 1984 National Merit Scholarship Program Finalist  
 1984 Bausch and Lomb Honorary Science Award  
 1984 Bank of America Achievement Award

1987 Letter of Commendation for Excellence in Biology Laboratory, Stanford University

**Honors** (continued)

1988 B.S., Biological Sciences with Honors, Stanford University  
 1990 Scholarship, American Medical Association  
 1988-1992 Scholarship, Indiana University  
 1992 Academic Achievement Award, Indiana University School of Medicine  
 1992 Citation for Research in Medical Science, Indiana University School of Medicine  
 1992-1995 Delegate, American Medical Association Resident Physician Section  
 1998 Pharmacia and Upjohn Research Award, UCLA Medical Center  
 1999-present Scientific Review Committee, Indiana University Cancer Center  
 2001 Grant Review Committee, Indiana University Cancer Center  
 2001-2002 Merit Review, Veterans Affairs Medical Research Service  
 2003-2007 Medical Advisory Board, Leukemia Research Foundation  
 2005 Reviewer for Genes, Chromosomes, and Cancer  
 2005 Reviewer for Journal of Leukocyte Biology

**B. Selected peer-reviewed publications (in chronological order)**

1. Zhi X, **Chan EM**, and Edenberg HJ. Tissue-specific regulatory elements in the human alcohol dehydrogenase 6 gene. *DNA and Cell Biology* 19:487, 2000.

2. **Chan EM\***, Comer EM, Brown FC, Richkind KE, Holmes ML, Chong BH, Shiffman R, Zhang D, Slovak ML, Willman CL, Noguchi CT, Li Y, Heiber DJ, Kwan L, Chan RJ, Vance GH, Ramsey HC, and Hromas RA. AML1-FOG2 Fusion Protein in Myelodysplasia. *Blood*. 2005; 105:4523-4526. Prepublished on February 10, 2005, as DOI 10.1182/blood-2004-07-2762.

\*-Corresponding author.

**C. Research Support**

**Ongoing Research Support**

Research Core Pilot Grant	(PI: Chan)	7/24/02 – present
Indiana University School of Medicine		(No cost extension)
Genetic Alterations in Leukemia		
Annual Direct Costs: \$10,000		
The goal of this study is to develop a mouse model of acute myeloid leukemia.		

VFR-175	(PI: Chan)	5/1/04 – 4/30/06
Clarian Health Partners		
Transcriptional Repression by the AML1-FOG2 Fusion Protein in Myelodysplastic Syndrome		
Annual Direct Costs: \$40,000		
The goal of this study is to determine the molecular mechanisms by which AML1-FOG2 functions as a transcriptional repressor.		

Young Investigator Award	(PI: Chan)	7/1/05 – 6/30/06
Department of Veterans Affairs		

## Distinct Hematopoietic Effects of the AML1-FOG2 and FOG2-AML1 Fusion Proteins in Myelodysplasia

Annual Direct Costs: \$25,000

The goal of this study is to determine whether AML1-FOG2 blocks differentiation in murine embryonic stem cells and if FOG2-AML1 transforms hematopoietic progenitors.

Translational Research Grant (Co-PI: Chan)

8/11/05 – 8/10/06

Indiana University Cancer Center

Epigenetic Changes in Myelodysplastic Syndromes

Annual Direct Costs: \$18,000

The goal of this study is to determine if aberrant methylation of genes in low-risk myelodysplastic syndromes impairs erythroid differentiation in an *in vitro* culture system.

**Pending Research Support**

Young Investigator's Grant (PI: Chan)

1/1/06 – 12/31/07

The Myelodysplastic Syndromes Foundation

Cooperative Disruption of Two Key Developmental Pathways in Myelodysplastic Syndromes

Annual Direct Costs: \$20,000

The goal of this study is to determine whether AML1-FOG2 blocks differentiation of murine bone marrow progenitors by recruiting the corepressor CtBP and induces pathologic features of myelodysplasia in mice.

Hoosier Oncology Group (Co-PI: Chan)

Not yet determined

A Phase II Trial of A Modified Dose and Schedule of Subcutaneously Administered Vidaza® (Azacitidine) and Erythropoietin in Patients with Low-risk Myelodysplastic Syndromes (less than 11% Marrow and Peripheral blood Blasts): Hoosier Oncology Group MDS04-85.

Annual Direct Costs: Not yet determined

The goal of the translational studies is to determine if azacitidine restores erythropoiesis by activating expression of the transcription factor GATA1 in the bone marrow of patients with low-risk MDS.

National Institutes of Health (NHLBI) (PI: Chan)

7/1/06 – 6/30/11

Role of FOG2 in the Pathogenesis of Myelodysplasia

Annual Direct Costs: \$100,000

The goal of this study is to determine whether AML1-FOG2 blocks hematopoietic development by disrupting the CBF and GATA pathways and induces myelodysplasia in mice.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Rebecca Jeanne Chan, M.D.-Ph.D.		POSITION TITLE Assistant Research Professor	
eRA COMMONS USER NAME RCHAN@IUPUI.EDU			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Indiana University, Bloomington, IN	B.S.	1984-1988	Biology
Indiana Univ. School of Med., Indianapolis, IN	Ph.D.	1995	Biochem and Mol. Biol.
Indiana Univ. School of Med., Indianapolis, IN	M.D.	1995	Medicine
UCLA School of Med., Los Angeles, CA	Resident	1995-1998	Internal Medicine
Indiana Univ. School of Med., Indianapolis, IN	Fellow	1998-1999	Hematology/Oncology
Indiana Univ. School of Med., Indianapolis, IN	Post-Doc	1999-2002	Hematology

**NOTE: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.**

**A. Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

- 1995-1998 Resident Physician, Department of Medicine, UCLA Medical Center  
Supervisor: Jan Tillisch, M.D.
- 1998-1999 Clinical Fellow, Division of Hematology/Oncology, Indiana University School of Medicine  
Supervisor: Lawrence Einhorn, M.D.
- 1999-2002 Post-Doctoral Fellow, Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Supervisor: Mervin C. Yoder, M.D.  
Supported by Individual National Research Service Award F32 CA84677
- 2002-2003 Assistant Scientist, Department of Pediatrics, Indiana University School of Medicine  
Supervisor: Richard Schreiner, M.D.
- 2004-pres. Assistant Research Professor, Departments of Pediatrics and of Medical and Molecular Genetics, Indiana University School of Medicine, Supervisor: Richard Schreiner, M.D.

**Honors**

- 1987 Phi Beta Kappa
- 1992 National Student Research Forum, Cell Biology/Human Genetics Award
- 1992 Midwest Student Medical Research Forum, First Place, Oral Presentation
- 1992-1995 Pre-Doctoral National Research Service Award, F30 AA05344
- 1994 Dr. Helen Sisson Scholarship, Merit-based
- 1995 Alpha Omega Alpha
- 1995 John B. Hickam Award for Excellence in Internal Medicine
- 1998 Diplomat, American Board of Internal Medicine (182250)
- 1999 Fellow's Merit Award, American Society of Clinical Oncology
- 2000 SmithKline Beecham Fellows' Forum, First Place, Oral Presentation
- 2000-2003 Post-Doctoral National Research Service Award, F32 CA84677

**B. Selected peer-reviewed publications (in chronological order).** Do not include publications submitted or in preparation.

1. Chan, R.J., AW McBride, HR Thomasson, A Ykenney, and DW Crabb. 1994. Allele frequencies of the preproenkephalin A (PENK) gene CA repeat in Asians, African-Americans, and Caucasians: Lack of evidence for different allele frequencies in alcoholics. *Alcoholism: Clin. Exp. Res.* 18, 533-5.

2. Chan, RJ, AW McBride, and DW Crabb. 1994. Seven transmembrane domain receptor subtypes identified in NG108-15 cells by reverse transcription-polymerase chain reaction. *Biochem. Biophys. Res. Comm.* **205**, 1311-7.
3. Hawes, JW, DW Crabb, RJ Chan, PM Rougraff, and RA Harris. 1995. Chemical modification and site-directed mutagenesis studies of rat 3-hydroxyisobutyrate dehydrogenase. *Biochem.* **34**, 4231-7.
4. Crabb, DW, MJ Stewart, and RJ Chan. 1996. Dexamethasone represses phorbol ester-, forskolin- and calcium-stimulated expression of the preproenkephalin A promoter-chloramphenicol acetyltransferase gene via a receptor-mediated mechanism. *Mol. Brain Res.* **42**, 103-8.
5. Chan, RJ, MJ Stewart, and DW Crabb. 1997. A direct repeat (DR-1) element in the first exon modulates transcription of the preproenkephalin A gene. *Mol. Brain Res.* **45**, 50-8.
6. Ganjoo, KN, RJ Chan, M Sharma, and LH Einhorn. 1999. Positron emission tomography scans in the evaluation of postchemotherapy residual masses in patients with seminoma. *J. Clin. Onc.* **17**, 3457-60.
7. Palis, J, RJ Chan, A Koniski, R Patel, M Starr, and MC Yoder. 2000. Spatial and temporal emergence of high proliferative potential hematopoietic precursors during murine embryogenesis. *Proc. Nat. Acad. Sci. USA* **98**, 4528-33.
8. Chan, RJ, X Xie, and MC Yoder. 2002. Thrombopoietin acts synergistically with leukemia inhibitory factor to maintain an undifferentiated state of embryonic stem cells homozygous for a Shp-2 deletion mutation. *FEBS Letters* **259**, 361-64.
9. Xie, X, RJ Chan, SA Johnson, M Starr, R Kapur, and MC Yoder. 2003. Thrombopoietin promotes mixed lineage and megakaryocytic colony forming cell growth but inhibits primitive and definitive erythropoiesis in cells isolated from early murine yolk sacs. *Blood* **101**, 1329-35.
10. Chan, RJ, SA Johnson, Y Li, MC Yoder, and G-S Feng. 2003. A Definitive Role of Shp-2 Tyrosine Phosphatase in Mediating Embryonic Stem Cell Differentiation to Mesoderm. *Blood* **102**, 2074-80.
11. Guo, Y, RJ Chan, H Ramsey, W Li, X Xie, WC Shelley, J Pedro Martinez-Barbera, B Bort, K Zaret, MC Yoder, and R Hromas. 2003. The Homeoprotein Hex is Required for Hemangioblast Differentiation. *Blood* **102**, 2428-35.
12. Zhong, L, W Li, Z Yang, M Tan, J Hansen, Y Li, RJ Chan, D Bischof, N Maina, KA Weigel-Kelley, W Zhao, SH Larsen, MC Yoder, W Shou, A Srivastava. 2004. Impaired nuclear transport and uncoating limit recombinant adeno-associated virus 2 vector-mediated transduction of primary murine Hematopoietic cells. *Human Gene Therapy* **15**, 1207-18.
13. Zhong, L, L Chen, Y Li, K Qing, KA Weigel-Kelley, RJ Chan, MC Yoder, and A Srivastava. 2004. Self-complementary adeno-associated virus 2 (AAV)-T cell protein tyrosine phosphatase vectors as helper viruses to improve transduction efficiency of conventional single-stranded AAV vectors in vitro and in vivo. *Molecular Therapy* **10**, 950-7.
14. Li, Y, JN McClintick, L Zhong, HJ Edenberg, MC Yoder, and RJ Chan\*. 2005. Murine embryonic stem cell differentiation is promoted by SOCS-3 and inhibited by the zinc finger transcription factor Klf4. *Blood* **105**, 635-7. \*CORRESPONDING AUTHOR
15. Chan, RJ\*, M Leedy, V Munugalavadla, CS Voorhorst, Y Li, M Yu, R Kapur. 2005. Human somatic *PTPN11* mutations induce hematopoietic cell hypersensitivity to granulocyte-macrophage colony stimulating factor. *Blood* **105**, 3737-42. \*CORRESPONDING AUTHOR
16. Chan, E, E Comer, F Brown, K Richkind, M Holmes, B Chong, R Shiffman, D-E Zhang, M Slovak, C Willman, CT Noguchi, Y Li, D Heiber, L Kwan, R Chan, G Vance, H Ramsey, R Hromas. 2005. AML1-FOG2 Fusion Protein in Myelodysplasia. *Blood* **105**, 4523-6.

#### Book Chapters/Reviews/Editorials

1. Hawes, JW, DW Crabb, RJ Chan, PM Rougraff, R Paxton, and RA Harris. 2000. Mammalian 3-Hydroxyisobutyrate Dehydrogenase. In: *Methods in Enzymology*, Volume 324. Harris, R.A. and Sokatch, J.R. (eds.), New York: Academic Press.
2. Chan, RJ, M You, and G-S Feng. 2004. Identification of trans-acting factors by electrophoretic mobility shift assay. In: *Cytokine Protocols* (Methods in Molecular Biology Series, Volume 249). De Ley, M. (ed.), Humana Press, Totowa, NJ.
3. Chan, RJ and L Cripe. 2005. 12-O-tetradecanoylphorbol-13-acetate in Acute Myeloid Leukemia. *Leukemia Research* **29**, 1107-8.
4. Chan, RJ, R Hromas, and MC Yoder. 2005. The role of Hex in hemangioblast and hematopoietic development. *Methods in Molecular Biology Series* (invited and accepted).

**C. Research Support.** List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

### **Ongoing Research Support**

5-FY04-77 (Chan, PI) 2/1/04 – 1/31/06

March of Dimes

Basil O'Connor Award

A Shp-2 mutation in mice causing hematologic abnormalities similar to Noonan Syndrome patients.

The major goals of this study are to understand how Shp-2 mutations affect developmental hematopoiesis, hematopoietic stem cell function, and mast cell biology.

(Chan, PI) 7/15/05 – 7/14/06

Indiana University School of Medicine Core Pilot Grant

Generating a 'Knock-In' Mouse Bearing an Activating *Ptpn11* Mutation.

RO1 HL082981-01 (Chan, PI) 9/15/05 – 8/31/09

NIH/NHLBI

Activating *PTPN11* and *c-kit* Mutations in Myeloproliferation.

The purpose of this study is to determine the role of *PTPN11* and *c-kit* mutations in juvenile myelomonocytic leukemia and systemic mastocytosis, respectively.

### **Completed Research Support**

(Chan, PI) 12/01/04 – 08/31/05

The Cores Centers of Excellence in Molecular Hematology

Pilot Grant

Somatic *PTPN11* Gain-of-Function Mutations in GM-CSF-Stimulated Cell Growth and Leukemogenesis.

F32 CA84677 (Chan, PI) 5/1/00 – 4/30/03

NIH/NCI

Molecular Mechanisms of Hematopoiesis and Leukemia.

The object of this study was to determine the role of the protein tyrosine phosphatase, Shp-2, in the process of differentiation from embryonic stem cells to the hemangioblast, a multi-potential cell with capacity to differentiate to both hematopoietic and endothelial cells, and to hematopoietic progenitors.

F30 AA05344 (Chan, PI) 7/15/92 – 7/14/95

NIH/NIAAA

Regulation of Preproenkephalin A Gene Expression and Possible Role in Alcoholism.

The object of this study was to understand the role of enkephalins in alcohol drinking behavior. We addressed this question by characterizing the preproenkephalin A promoter and by looking for associations between the preproenkephalin A locus and drinking behavior in humans.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME <b>Cheong-Hee Chang, Ph.D.</b>		POSITION TITLE	
eRA COMMONS USER NAME chechang		Associate Professor	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Seoul National University, Korea	B.S.	1977	Food and Nutrition
Seoul National University, Korea	M. S.	1982	Biology
University of Virginia, Charlottesville, VA	Ph. D.	1990	Biology
Yale School of Medicine, New Haven, CT			Immunology

**A. Professional Experience**

- 1994-1996 Research Associate, Section of Immunobiology, Yale School of Medicine, New Haven, CT.
- 1996-2001 Assistant Professor, Department of microbiology and Immunology, University of Michigan Medical School, Ann Arbor, MI.
- 2001-present Associate Professor, Department of microbiology and Immunology, Indiana University School of Medicine, Indianapolis, IN.
- 1999-2003 Associate Editor, J. Immunology
- 2000-2003 Member, American Heart Association study section (national)
- 2001-2004 Executive Council Member, Autumn Immunology Conference
- 2004-present Member, NIH Cellular and Molecular Immunology-B study section

**B. Honors and Awards**

- 1998 Travel Award, American Association of Immunologists
- 1999 Excellence in Teaching Award, U. Michigan
- 2000 Faculty Career Development Award. U. Michigan Medical School
- 2001 Teacher of the month, U. Michigan Medical School
- 2005 Trustee Teaching Award, Indiana University School of Medicine

**C. Publications**

- Cheong-Hee Chang, Juergen Hammer, Johnson E. Loh, William L. Fodor, and Richard A. Flavell. 1992, The activation of major histocompatibility complex class I genes by interferon regulatory factor-1 (IRF-1). Immunogenetics 35:378-384.
- Cheong-Hee Chang, William L. Fodor, and Richard A. Flavell. 1992. Reactivation of a major histocompatibility complex class II gene in mouse plasmacytoma cells and mouse T cells. J. Exp. Med. 176:1165-1169.
- Johnson E. Loh, Cheong-Hee Chang, William L. Fodor, and Richard A. Flavell. 1992. Dissection of the interferon- $\gamma$ -MHC class II signal transduction pathway reveals that type I and type II interferon systems share common signaling component(s). EMBO J. 11:1351.

4. Cheong-Hee Chang, Joseph Fontes, Matija Peterlin and Richard A. Flavell. 1994. CIITA is sufficient for the inducible expression of MHC class II genes. J. Exp. Med. 180:136.
5. Cheong-Hee Chang and Richard A. Flavell. 1995. CIITA regulates the expression of multiple genes involved in antigen presentation. J. Exp. Med. 181:765.
6. Cheong-Hee Chang, Soon-Cheol Hong, Christopher Hughes, Charles Janeway, Jr. and Richard A. Flavell. 1995. CIITA activates the expression of MHC class II genes in mouse T cells. Int. Immunol. 7:1515.
7. Cheong-Hee Chang, Sylvie Guerder, Soon-Cheol Hong, Willem van Ewijk and Richard A. Flavell. 1996. Mice lacking the MHC class II transactivator (CIITA) show tissue specific impairment of MHC class II expression. Immunity 4:167.
8. Lynn Soong, Cheong-Hee Chang, Jiaren Sun, B. Jack Longley, Jr., Nancy H. Ruddle, Richard A. Flavell and Diane McMahon-Pratt. 1997. Role of CD4<sup>+</sup> T cells in pathogenesis associated with *Leishmania amazonensis* infection. J. Immunol. 158:5374.
9. Erol Fikrig, Stephen W. Barthold, Manchuan Chen, Cheong-Hee Chang and Richard A. Flavell. 1997. Protective antibodies develop, and murine Lyme arthritis regresses, in the absence of MHC class II and CD4 T cells. J. Immunol. 159:5682.
10. G. Stuart Williams, Mark Malin, David Vremec, Cheong-Hee Chang, Richard Boyd, Christophe Benoist and Diane Mathis. 1998. Mice lacking the transcription factor CIITA—a second look. Int. Immunol. 10: 1957-1967.
11. Tania Gourley, Stacey Roys, Nick Luckas, Steven Kunkel, Richard A. Flavell and Cheong-Hee Chang. 1999. A novel role for the major histocompatibility complex class II transactivator CIITA in the repression of IL-4 production. Immunity. 10: 377-386.
12. Conchi Mora, F. Susan Wong, Cheong-Hee Chang and Richard A. Flavell. 1999. Pancreatic infiltration but not diabetes occurs in the relative absence of MHC class II-restricted CD4 T cells: Studies using NOD/CIITA-deficient mice. J. Immunol. 162: 4576-4588.
13. Cheong-Hee Chang, Stacey Roys and Tania Gourley. 1999. Class II transactivator (CIITA): Is it a master switch for MHC class II gene expression? Microbes and Infection. 1: 879-885.
14. Tyler Sisk, Tania Gourley, Stacey Roys and Cheong-Hee Chang. 2000. CIITA inhibits IL-4 gene transcription by competing NFAT to bind CBP/p300. J. Immunol. 165:2511.
15. Mohammed Saifuddin, Gregory T. Spear, Cheong-Hee Chang, and Kenneth A. Roebuck. 2000. Expression of the MHC class II molecule HLA-DR in T cells is associated with higher HIV-1 expression. Clin. Exp. Immunol. 121: 324-331.
16. Mohammed Saifuddin, Kenneth A. Roebuck, Cheong-Hee Chang, Jenny P. Y. Ting and Gregory T. Spear. 2000. Activation of HIV-1 transcription by the MHC class II transactivator. Cutting Edge, J. Immunol. 164:3941-3945.
17. Tania Gourley and Cheong-Hee Chang, 2000. The class II transactivator prevents activation-induced cell death by inhibiting Fas ligand gene expression. Cutting Edge, J. Immunol. 166:2917-2921.
18. Zhu A. Cao, Bethany B. Moore, David Quezada, Cheong-Hee Chang, Patricia P. Jones. 2000. Identification of an IFN- responsive region in an intron of the invariant chain gene. Eur. J. Immunol. 30: 2604-2611.
19. Kevin Nickerson, Tyler J. Sisk, Naohiro Inohara, Christina S. K. Yee, Jennifer Kennell, Min-Chul Cho, P. Joseph Yannie II, Gabriel Nunez, and Cheong-Hee Chang. 2001. Dendritic cell specific CIITA contains a caspase-recruitment domain that confers potent transactivation activity. J. Biol. Chem. 276:19089-19093.
20. Tyler Sisk, Stacey Roys, and Cheong-Hee Chang, 2001. Self-association of CIITA and its transactivation potential. Mol. Cell. Biol. 21:4919-4928.

21. Tania Gourley, Dipak Patel, Kevin Nickerson, Soon-Cheol Hong, and Cheong-Hee Chang, 2002. Aberrant expression of Fas ligand in mice deficient for the MHC class II transactivator (CIITA). J. Immunol. 168:4414-4419.
22. Cheong-Hee Chang, Tania Gourley, and Tyler Sisk, 2002. Function and regulation of class II transactivator in the immune system. Immunol. Res. 25:131.
23. Tyler Sisk, Kevin Nickerson, Roland Kwok, and Cheong-Hee Chang, 2003. Phosphorylation of CIITA regulates CIITA interaction and function. Int. Immunol. 15: 1195-1205.
24. Lai, W., Chang, C.-H., and Farber, D.L. 2003. Gene Transfection and Expression in resting and activated murine T cell subsets. J. Immunol. Meth. 282: 93-102.
25. Kamel Benlagha, Se-Ho Park, Rodolphe Guinamard, Claire Forestier, Lars Karlsson, Cheong-Hee Chang, and Albert Bendelac. 2004. Mechanisms Governing B Cell Developmental Defects in Invariant Chain-Deficient Mice. J. Immunol. 172:2076-2083.
26. Christina Yee, Yongxue Yao, Janice Blum, and Cheong-Hee Chang. 2004. Cathepsin E: a novel target of regulation by Class II transactivator (CIITA). J. Immunol. 172: 5528-5534.
27. Dipak Patel, Mark Kaplan, and Cheong-Hee Chang. 2004. Altered Th1 cell differentiation programming by CIITA deficiency. J. Immunol. 173:5501-5508.
28. Christina S.K. Yee, Yongxue Yao, Qi Xu, Brian McCarthy, Deqin Sun-Lin, Masahide Tone, Herman Waldmann, and Cheong-Hee Chang. 2005. Enhanced Production of IL-10 by Dendritic Cells Deficient in CIITA. J. Immunol. 174:1222-1229.
29. Csencsits K, Sherri C. Wood, Guanyi Lu, John C. Magee, Ernst J. Eichwald, Cheong-Hee Chang, and D. Keith Bishop. 2005. Graft rejection mediated by CD4+ T cells via indirect recognition of alloantigen is associated with a dominant Th2 response. Eur. J. Immunol. 35:843-851.
30. Sarita Sehra, Dipak Patel, Saritha Kusam, Zheng-Yu Wang, Cheong-Hee Chang, and Alexander L. Dent. 2005. A Role for Caspases in Controlling IL-4 Expression in T cells. J. Immunol. 174: 3440-3446.
31. Dipak R. Patel, Wei Li, Jae-Seung Park, Tania S. Gourley, Gaio Hangoc, Mark H. Kaplan, and Cheong-Hee Chang. 2005. Constitutive expression of CIITA predisposes CD4 T cells to produce Th2 cytokines. Cell. Immunol. 233:30-40.
32. Yongxue Yao, Wei Li, Mark Kaplan and Cheong-Hee Chang. 2005. IL-4 inhibits IL-10 to promote IL-12 production by dendritic cells. J. Exp. Med. 201:1899-1903.
33. Wei Li, Moon G. Kim, Tania S. Gourley, Derek Sant'Angelo, and Cheong-Hee Chang. MHC class II expression in thymocytes is sufficient to mediate CD4 T cell selection. Immunity. In press.
34. Li, P., N. Wang, D. Zhou, C.S.K. Yee, C-H. Chang, R. Brutkiewicz, and J.S. Blum. Disruption of MHC class II-restricted antigen presentation by vaccinia virus. J. Immunol. In press.
35. Thorsten Buch, Bojan Polic, Björn E. Clausen, Judith Alferink, Susanne Weiss, Özlem Akilli, Cheong-Hee Chang, Richard Flavell, Stipan Jonjic, Ari Waisman and Irmgard Förster. MHC class II expression through a hitherto unknown pathway supports T helper cell dependent immune responses: implications for Bare Lymphocyte Syndrome. Under revision (Blood).
36. Jessica L. Claybrook, Dipak Patel, Edwin S. Colvin, Sung-Yoo Cho, Randy R. Brutkiewicz, Cheong-Hee Chang, and Soon-Cheol Hong. Modulation of Cytokine Production by Vaccinia Virus A52R. Under revision (J. Immunol).
37. Allison T. Thiele, Tina L. Sumpter, Joanna A. Walker, Qi Xu, Cheong-Hee Chang, Robert L. Bacallao, and David S. Wilkes. Pulmonary Immunity to Viral Infection: Adenovirus Infection of Lung Dendritic Cells Renders T cells Non-Responsive to IL-2. Under revision (J. Virol).
38. Soo Jung Yang, Sejin Ahn, Chan Sik Park, Cheong-Hee Chang, Kevin Holmes, and Moon G. Kim. Quantity of MHC II on thymic epithelium is not limiting for thymocyte development during postnatal age. Submitted.

39. Myung-Ja Kwon, Jae-Won Soh, and Cheong-Hee Chang. Protein Kinase C delta is essential to maintain CIITA gene expression in B cells. Submitted.
40. Zhao, Q., Wang, X., Nelin, L. D., Yao, Y., Manson, M. E., Baliga, R., Meng, X., Smith, C. V., Bauer, J. A., Chang, C.-H., and Y. Liu. The role of MAP kinase phosphatase 1 in regulating LPS stimulated innate immune responses. Submitted.

## Research Support

RO1 AI45811 (PI)

05/01/01-04/30/06

NIAID

Title: The regulation and function of CIITA in CD4 T cells

The goal of this project is to study how CIITA regulates T helper cell differentiation programming. The competitive renewal application has been submitted. No overlap with the current application.

RO1 AI53556 (PI)

05/15/02-04/30/06

NIAID

Title: MHC class II transactivator function and regulation

The goal of this project is investigating how CIITA function is regulated by PKA mediated phosphorylation. This project will not be renewed. No overlap with the current application.

PO1 AI056097

09/01/03-02/31/08

NIAID (PI of the Program, Project 2 and the Administrative Core)

Title: Poxvirus modulation of immune responses

The program project is investigating how vaccinia virus modulates antigen presentation function of hosts. Project 2 focuses on gene regulation and signaling pathways that are targeted by vaccinia virus. No overlap with the current application.

0520111Z (Mentor for Yongxue Yao)

1/1/05-12/31/06

American Heart Association (Postdoctoral fellowship)

Title: Role of interleukin-4 in dendritic cell-mediated immune responses.

The goal of this project is to understand how IL-4 regulates IL-10 gene expression in DC. No overlap with the current application.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed for Form Page 2.  
Follow the sample format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME		POSITION TITLE	
Tien-Min Gabriel Chu		Assistant Professor	
eRA COMMONS USER NAME			
tgchu1			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Kaohsiung Medical University, Taiwan	DDS	1989	Dentistry
University of Michigan, Ann Arbor, Michigan	PhD	1999	Materials Sci. & Eng.
University of Michigan, Ann Arbor, Michigan	Post-Doc	2001	Biomed. Engineering

**A. Positions and Honors**

## Position

- 1999 - 2001 Post-Doc research fellow, Department of Material Sciences and Engineering, College of Engineering, University of Michigan
- 1999 - 2000 Adjunct Lecturer, Department of Biological and Materials Sciences, Division of Prosthodontics, School of Dentistry, University of Michigan
- 2000 - 2002 Adjunct Assistant Professor, Department of Biological and Materials Sciences, Division of Prosthodontics, School of Dentistry, University of Michigan
- 2001 - 2002 Assistant Research Scientist, Department of Biomedical Engineering, College of Engineering, University of Michigan
- 2003 - Assistant Professor, Biomedical Engineering Program, Indiana University Purdue University Indianapolis

**B. Selected Peer-Reviewed Publication (13 papers and 4 US Patent)**

- Tien-Min G. Chu and Rena L. Stewart "Biodegradable load-bearing carrier for bone regeneration" (US patent pending, Ice Miller Ref. No. P01243-US-00, US PTO #60/652,537)
- Hollister, Scott J., Gabriel Tien-Min; Taboas, Juan M, "Design methodology for tissue engineering scaffolds and biomaterial implants" (US patent pending, Pub. App. No. 20030069718)
- Taboas, Juan M; Maddox, Rachel D.; Krebsbach, Paul H., Scott J., Tien-Min Gabriel "Controlled local/global and micro/macro-porous 3D plastic, polymer and ceramic/cement composite scaffold fabrication and applications thereof" (US Patent Pending, Pub. App. No. 20030006534)
- T-M. G. Chu "Solid Freeform Fabrication of Tissue Engineering Scaffolds" in Scaffolding in Tissue Engineering, Eds. X. Ma and J. Eliseeff, Marcel Dekker, Inc., 2005 p.139-154
- Hollister, S.J., Taboas, J.M., Schek, R.M., Lin, C.Y., and Chu, T.M. (2004) "Design and Fabrication of Bone Tissue Engineering Scaffolds" in Bone Tissue Engineering, Eds, Hollinger et al. CRC Press LLC. P. 167-192

6. T-M. G. Chu, D.G. Orton, J.W. Halloran, S.J. Hollister, S.E. Feinberg, "Mechanical and in vivo performance of hydroxyapatite implants containing controlled internal architecture" *Biomaterials* **23** (2002) p.1283-1293
7. T-M. G. Chu, J.W. Halloran, S.J. Hollister, S.E. Feinberg, "Hydroxyapatite implants with controlled internal architecture" *Journal of Materials Science: Materials in Medicine* **12** (2001) p.471-478
8. S.E. Feinberg, S.J. Hollister, J.W. Halloran, T.M.G. Chu, and P.H. Krebsbach, "Image-Based Biomimetic approach to reconstruction of the temporomandibular joint" *Cells Tissues Organs* **163** (2001) p.309-321
9. Hollister, S.J., Zysset, P.K., Guldborg, R.E., Chu, T.M. and Halloran, J.W. "Engineering microstructures to evaluate and replace trabecular bone." *Adv Exp Med Biol* **496** (2001) p.199-211.
10. T-M. G. Chu, and J.W. Halloran, "High-Temperature Flow Behavior of Ceramic Suspensions" *Journal of the American Ceramic Society* **83** (2000) p.2189-2195
11. T-M. G. Chu and J.W. Halloran, "Curing of highly-loaded ceramic suspensions in acrylates" *Journal of the American Ceramic Society* **83** (2000) p.2375-2380
12. S.J. Hollister, T.M. Chu, R.A. Levy, J.W. Halloran, and S.E. Feinberg, "An Image-Based Approach for Designing and Manufacturing Craniofacial Scaffolds" *International Journal of Oral and Maxillofacial Surgery* **29** (2000) p.67-71
13. S.E. Feinberg, S.J. Hollister, J.W. Halloran, T.M. Chu, and P.H. Krebsbach, "A tissue engineering approach to site-specific reconstruction of skeletal structures of the maxillofacial region: Part I" *Shanghai Journal of Stomatology* **9** (2000) p.36-40
14. S.E. Feinberg, S.J. Hollister, J.W. Halloran, T.M. Chu, and P.H. Krebsbach, "A tissue engineering approach to site-specific reconstruction of skeletal structures of the maxillofacial region: Part II" *Shanghai Journal of Stomatology* **9** (2000) p.88-93
15. M.L. Griffith, J.W. Halloran, and T.M. Chu, US Patent 6,117,612 "StereoLithography Resin for Rapid Prototyping of Ceramics and Metals"
16. R. Levy, T.M. Chu, J.W. Halloran, S.E. Feinberg, and S. Hollister, "CT-Generated Porous Hydroxyapatite Orbital Floor Prosthesis as a Prototype Bioimplant" *American Journal of Neuroradiology AJNR* **18** (1997) p. 1522-1525
17. W. Wagner and T.M. Chu, "Biaxial flexural strength and indentation fracture toughness of three new dental core ceramics" *Journal of Prosthetic Dentistry* **76** (1996) p.140-144

## C. Research Support

### Current Research Project

1 R03 EB005426-01(NIBIB/NIH), Chu (PI) 9/1/2005 - 8/31/2007  
Development of a biodegradable, load-bearing DBM carrier  
Role: PI

1 R01 EB003162-01 (NIBIB/NIH). Xie (PI) 7/1/2005 – 8/31/2006  
Novel Amino Acid-Based Glass-Ionomer Biomaterials  
Role: Investigator

### Completed Research Project

RO1 DE13608 (NIDCR/NIH) Scott Hollister (PI) 1/1/2003 - 9/14/2003  
Engineering Joint Scaffolds for Concurrent Function and Regeneration  
Role: Investigator

**BIOGRAPHICAL SKETCH**

NAME <b>Matthias A. Clauss, Ph.D.</b>		POSITION TITLE <b>Associate Professor of Integrative and Cellular Physiology</b>	
EDUCATION/TRAINING ( <i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i> )			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Albert Einstein University, Ulm, Germany	Diploma	1982	Chemistry
Ruprecht Karls University, Heidelberg, Germany	Ph.D.	1988	Biology
Columbia University, New York, NY, USA	Postdoctoral	1991	Physiology
Philipps University, Marburg, Germany	Habilitation	1997	Molecular Cell Biology & Biochemistry

**A. Positions and Honors****Positions:**

**Postdoctoral research fellow** (1988 to 1991) Columbia University, New York, Department of Physiology and Cellular Biophysics, Principal investigator: Dr. David Stern

**Research Associate** (1991) Columbia University, New York, Department of Physiology and Cellular Biophysics, Principal investigator: Dr. David Stern

**Researcher** (1992 to 1994) Max-Planck-Institute of Neurobiology in Martinsried, Germany

**Principal Investigator** (1994 to 2003) Max-Planck-Institute of "Physiological and Clinical Research", Germany, Directors: Dr. Werner Risau, Dr. Wolfgang Schaper

**Associate Professor and Member** (2003 to present), Department of Cellular & Integrative Physiology, Indiana Center for Vascular Biology & Medicine, Indiana University, Indianapolis

**Honors, Awards:**

**Helmholtz-Award for Neurobiology** (1992) by the BMBF

**B. Selected (26 out of 44) peer-reviewed publications (in chronological order)**

- Ogawa S, **Clauss M**, Shreeniwas R, Butura C, Koga S, Stern DM (1991) Hypoxia induces endothelial cell synthesis of novel membrane-associated proteins including a new activator of coagulation factor X. *Proc. Natl. Acad. Sci. U. S. A.* 88: 9897-9901
- Kao J, Ryan, J, Brett G, Chen J, Shen H, Fan Y-G, Godman G, Familetti PC, Wang F, Pan Y-CE, Stern D, **Clauss M** (1992) Endothelial-monocyte activating polypeptide II. A novel tumor-derived polypeptide that activates host-response mechanisms. *J. Biol. Chem.* 267: 20239-20247
- Shen H, **Clauss M**, Ryan J, Schmidt AM, Tijburg P, Borden L, Connolly D, Stern D, Kao J (1993) Characterization of vascular permeability factor/vascular endothelial growth factor receptors on mononuclear phagocytes. *Blood* 81: 2767-2773 (1. & 2. author contributed equally)
- Gerlach H, Gerlach M, **Clauss M** (1993) Relevance of tumor-necrosis-factor-alpha and interleukin-1-alpha in the pathogenesis of hypoxia-related organ failure. *Europ. J. Anaesth.* 10: 273-285
- Grell M, Douni E, Wajant H, Löhden M, **Clauss M**, Maxeiner B, Georgopoulos S, Lesslauer W, Kollias G, Pfizenmaier K, Scheurich P (1995) The transmembrane form of tumor necrosis factor (TNF) is the prime activating ligand of the 80 kDa TNF receptor. *Cell.* 83: 793-802
- Clauss M**, Weich H, Breier G, Knies U, Röckl W, Waltenberger J, Risau W (1996) The vascular endothelial growth factor receptor flt-1 mediates biological activities: Implications for a functional role of placenta growth factor in monocyte activation and chemotaxis. *J. Biol. Chem.* 271: 17629-17634
- Clauss M**, Grell M, Fangman C, Fiers W, Scheurich P, Risau W (1996) Synergistic induction of endothelial tissue factor by tumor necrosis factor and vascular endothelial growth factor: functional analysis of the tumor necrosis factor receptors. *FEBS Letters* 390: 334-338

8. Hippenstiel S, Krüll M, Ikemann A, Risau W, **Clauss M**, Suttorp N (1998) VEGF induces hyperpermeability by a direct action on endothelial cells. *Am. J. Physiol.* 274: L678-684
9. Knies UE, Behrendorf HA, Mitchell C, Deutsch U, Risau W, Drexler H, **Clauss M** (1998) Regulation of endothelial monocyte-activating polypeptide II-release by apoptosis. *Proc. Natl. Acad. Sci. U. S. A.* 95: 12322-12327
10. Meyer M, **Clauss M**, Lepple-Wienhaus A, Waltenberger J, Augustin HG, Ziche M, Lanz C, Büttner M, Rziha H-J, Dehio C (1999) A novel vascular endothelial growth factor encoded by Orf virus, VEGF-E, mediates angiogenesis via signalling through VEGFR-2 (KDR) but not VEGFR-1 (Flt-1) receptor tyrosine kinases. *EMBO J.* 18: 363-374
11. Fischer S, **Clauss M**, Wiesnet M, Renz D, Schaper W, Karliczek GF (1999) Hypoxia induces permeability in brain microvessel endothelial cells via VEGF and NO. *Am. J. Physiol.* 276: C812-820
12. Behrendorf HA, Van de Craen M, Knies UE, Vandenabeele P, **Clauss M** (2000) The endothelial monocyte-activating polypeptide II (EMAP II) is a substrate for caspase-7. *FEBS Letters* 466: 143-147
13. Knies UE, Kröger S, **Clauss M** (2000) Expression of EMAP II in the developing and adult mouse. *Apoptosis* 5: 141-151
14. Heil M, **Clauss M**, Buschmann IR, Willuweit A, Suzuki K, Fischer S, Schaper W (2000) Vascular endothelial growth factor (VEGF) stimulates monocyte migration through endothelial monolayers via increased integrin expression. *Eur. J. Cell Biol.* 79: 850-857
15. Mechtcheriakova D, Schabbauer G, Lucerna M, deMartin R, **Clauss M**, Binder BR, Hofer E (2001) Specificity, diversity and convergence in VEGF and TNF-alpha signaling events leading to tissue factor upregulation via EGR-1. *FASEB J.* 15: 230-242
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18. Willuweit A, Sass G, Schöneberg A, Eisel U, Tiegs G, **Clauss M** (2001) Chronic inflammation and protection from acute hepatitis in transgenic mice expressing tumor necrosis factor in endothelial cells. *J. Immunol.* 167: 3944-3952
19. Matschurat S, Knies UE, Person V, Fink L, Stoelcker B, Ebenebe C, Behrendorf HA, Schaper J, **Clauss M**. 2003 Regulation of EMAP II by Hypoxia. *Am J Pathol.* 162: 93-103
20. Issbrücker K, Marti HH Hippenstiel S, Springmann G, Voswinckel R, Gaumann A, Breier G, Drexler H, Suttorp N, **Clauss M** (2003) p38 MAPK - a molecular switch between angiogenesis and vascular permeability. *FASEB J.* 17: 262-264
21. Pipp F, Heil M, Issbrücker K, Ziegelhoeffer T, Martin S, van den Heuvel J, Weich H, Fernandez B, Schaper W, **Clauss M** (2003) The VEGFR-1 selective VEGF-homologue PIGF is arteriogenic: evidence for a monocyte mediated mechanism, *Circ. Res.* 92:378-385
22. Koczulla R., von Degenfeld G., Zahler S., Kroetz F., Gloe T., Issbrücker K., Lebherz C., Boekstegers P., Vogelmeier C., **Clauss M**, Bals R. (2003) An angiogenic role for the human peptide antibiotic LL-37/hCAP-18, *J. Clin. Invest.* 111: 1665-72
23. Matschurat S, Blum S, Dejkman H, Kanal L, de Waal R, **Clauss M** (2003) A negative regulatory of PI3-kinase in TNF-induced tumor necrosis. *Int. J. Cancer* 107: 30–37
24. Voswinckel R, Ziegelhöfer T, Heil M, Kostin S, Breier G, Deutsch U, Mehling T, Haberberger R, **Clauss M**, Gaumann A, Schaper W and Seeger W. (2003) Circulating vascular progenitor cells do not contribute to compensatory lung growth. *Circ. Res.* 93: 372-379
25. Heil M, Mittnacht-Krauss R, Issbrücker K, van den Heuvel J, Dehio C, Schaper W, **Clauss M** and Weich HA. (2004) An engineered heparin-binding form of VEGF-E (hbVEGF-E): Biological effects in vitro and mobilization of precursor cells. *Angiogenesis* 6: 201-11
26. Zohlnhofer D, Nuhrenberg TG, Neumann FJ, Richter T, May AE, Schmidt R, Denker K, **Clauss MA**, Schomig A, Baeuerle PA. (2004) Rapamycin effects transcriptional programs in smooth muscle cells controlling proliferative and inflammatory properties. *Mol Pharmacol.* 65(4):880-9

## C. Research Support

- Project:** Grant in-Aid for Research, PI  
**Source:** German Research Society (DFG)  
**Title:** Continuous endothelial activation by transmembrane TNF-expression  
**Major goals:** To study overexpression of endothelial transmembrane TNF
- Dates of Project (Entire Period of Support):  
2002 – 2003  
(ended because of move to USA)
- Project:** PPG 1069/ Grant in-Aid for Research, PI  
**Source:** German Research Society (DFG)  
**Title:** Dissection of angiogenesis and vascular hyperpermeability.  
**Major Goals:** Identification of signal transduction events induced by VEGF, which regulate angiogenesis and vascular permeability
- Dates of Project (Entire Period of Support):  
2002 – 2003  
(ended because of move to USA)
- Project:** PPG 547/ Grant in-Aid for Research, PI  
**Source:** German Research Society (DFG)  
**Title:** Role of EMAP II in cardio-pulmonal diseases  
**Major Goals:** Study of EMAP II regulation and generation of EMAP II transgenic animals
- Dates of Project (Entire Period of Support):  
1997 – 2003
- Project:** EC project/ Grant in-Aid for Research, PI  
**Source:** European Community  
**Title:** Targeting signaling mechanisms essential for angiogenesis  
Major Goals: Target signal transduction events of angiogenesis for anti-angiogenesis therapy of tumors
- Dates of Project (Entire Period of Support):  
2002 – 2003  
(ended because of move to USA)
- Project:** Grant in-Aid for Research, PI  
**Source:** Kerckhoff-Foundation  
**Title:** Recombinant expression of VEGF-homologies and soluble VEGF-receptors  
**Major Goals:** Production of VEGF-homologues for therapeutic arteriogenesis
- Dates of Project (Entire Period of Support):  
2001 – 2002

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Yansheng Du	POSITION TITLE Assistant Professor		
eRA COMMONS USER NAME ydu			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Beijing Normal University, Beijing, China	BS	1982	Biology
Beijing Medical University, Beijing, China	MS	1987	Cytogenetics
Wayne State University, School of Medicine, Detroit	Ph.D.	1994	Pathology

**A. Positions and Honors.****Positions and Employment**

1982-1984 Assistant to Lecturer in Biology Department, Beijing Educational Institute.

1984-1987 Teaching and research assistant in Radiomedicine Department, Beijing Medical University.

1988-1994 Teaching and research assistant in Department of Pathology, Wayne State University School of Medicine.

1994-1998 Post-doctoral scientist in Central Nervous System, Eli Lilly and Company.

1998-2002 Assistant scientist/assistant Professor in Dept. of Pharmacology and Toxicology, Indiana University School of Medicine.

2002-present Assistant Professor in Dept. of Neurology, Indiana University School of Medicine.

**Other Experience and Professional Memberships:**

1994-present Member, Society for Neuroscience

2002-present Member, Movement Disorder Society

**Honors:**

1. Guest Professor, Institute of Neuroscience, Beijing Medical University, 1998-present
2. Visiting Scientist, Eli Lilly and Company, 1998-2002
3. Affiliated Scientist, IU Center for Aging Research, 2003-present
4. Faculty, Graduate Program in Medical Neurobiology, Indiana University School of Medicine, Indianapolis, IN (2003-present)

**B. Selected peer-reviewed publications (Selected from 47 publications).**

1. Mao T.S., **Du Y.** et al; Familial Graves' Disease with HLA.. Chinese Journal of Internal Medicine. 27:352 - 354, 1988

2. Wang K., **Du Y.**, Diglio C., Tsang W., Kuo T. H.; Hormone-Induced Phosphorylation of the Plasma Membrane Calcium Pump in Cultured Aortic Endothelial Cells. Arch. Biochem. Biophys., 289:103 - 108, 1991

3. **Du Y.**, Carlock L., and Kuo T.H; The Mouse Plasma Membrane Ca Pump Isoform 1 Promoter: Cloning and Characterization. Arch. Biochem. Biophys., 316:309 - 312, 1995

4. Ni B., **Du Y.**, Rosteck P. Jr., Wu X., and Paul S. M.; Molecular cloning, expression and chromosomal localization of a Human brain-specific Na<sup>+</sup>-dependent inorganic phosphate cotransporter. J. Neurochem. 66:2227 - 2238, 1996

5. Ni B., Wu X., **Du Y.**, Hamilton-Byrd E., Bales K., Rosteck P Jr., Su Y., and Paul S. M.; Role of an ICE-like protease in KCl deficiency-mediated neuronal death. *J. of Neurosci.*, 17:1561-1569, 1997.
6. Ni B., Wu X., **Du Y.**, Hamilton-Byrd E., Bales K., Rosteck P Jr., Su Y, and Paul S. M.; Role of an ICE-like protease in KCl deficiency-mediated neuronal death. *Alzheimer's Disease: Biology, Diagnosis and Therapeutics*. Edited by K. Iqbal, B. Winblad, T. Nishimura, M. Takeda and H. M. Wisniewski. 485-490, 1997
7. **Du Y.**, Ni B., Glinn M., Dodel R., Bales K., Zhang Z., Hyslop P. and Paul S. M.;  $\alpha_2$ -Macroglobulin as an Amyloid  $\beta$  Peptide Binding Plasma Protein. *J. Neurochem*, 69:299-305, 1997
8. **Du Y.**, Dodel R., Bales K., Hamilton-Byrd E., and Paul S. M.. Involvement of a Caspase-3-like Cysteine Protease in 1-Methyl-4-Phenylpyridinium (MPP<sup>+</sup>) mediated Apoptosis of Cultured Cerebellar Granule Neurons. *J. Neurochem*. 69: 1382-1388, 1997
9. **Du Y.**, Bales K., Dodel R., Hamilton-Byrd E., Horn J., Ni B. and Paul S. M.. Activation of CPP 32/Apopain is Required for Glutamate-mediated Neuronal Apoptosis. *Proc. Natl. Acad. Sci. USA* 94: 11657-11662, 1997
10. Bales K., Verina T., Dodel R., **Du Y.**, Altstiel L., Bender M., Hyslop P., Johnstone E., Little S., Cummins D., Piccardo P., Ghetti B., and Paul S. M.. Lack of apolipoprotein E dramatically reduces amyloid  $\beta$ -peptide deposition. *Nature Genetics* 17: 263-264, 1997
11. **Du Y.**, Bales K. R., Dodel R. C., Liu X, Glinn M. A., Horn J. W., Little S. P. and Paul S. M..  $\alpha_2$ -Macroglobulin Attenuates A $\beta$ (1-40) Fibril Formation and Associated Neurotoxicity of Cultured Fetal Rat Cortical Neurons. *J. Neurochem*. 70: 1182-1188, 1998
12. Bales K., **Du Y.**, Dodel R., Yan GM, Hamilton-Byrd E., and Paul S. M.. The NF- $\kappa$ B/Rel Family of Proteins Mediates A $\beta$ -Induced Neurotoxicity and Glial Activation. *Brain Res Mol Brain Res* 57:63-72, 1998
13. Dodel R., **Du Y.**, Bales K., Ling Z-D, Carvey P. M., Paul S. M.. Peptide inhibitors of caspase-3-like proteases attenuate MPP<sup>+</sup>-induced toxicity of cultured fetal rat mesencephalic dopamine neurons. *Neuroscience* 86:701-707, 1998
14. Dodel R., **Du Y.**, Bales K., Paul S. M... Caspase 3 and 6-hydroxydopamine-induced neuronal apoptosis. *Brain Res. Mol. Brain Res*. 64:141-148, 1999
15. Dodel R., Bales K., Farlow M., Gasser T., Paul S.M., **Du Y.**.. Rapid Detection of a Pentanucleotide Deletion Polymorphism in the Human  $\alpha_2$ -Macroglobulin Gene. *Clin. Chem*. 45:307, 1999
16. Dodel R., **Du Y.**, et al. Sodium Salicylate and 17- $\beta$ -Estradiol Attenuate Nuclear NF- $\kappa$ B Translocation in Cultured Rat Astroglial Cultures Following Exposure to Amyloid Ab(1-40) and Lipopolysaccharides. *J. Neurochem*. 73, 1453-1460, 1999.
17. Liu, X., Clemens, J.A., Yin, T., Stephenson, D.T., Johnstone, E.M., **Du, Y.**, Paul, S.M., and Little, S.P. Rat B2 sequences are induced in the hippocampal CA1 region after transient global cerebral ischemia. *J. Biol. Chem*. 274(40):28674-81, 1999
18. Bales, KR., Verina, T, Cummins, DJ., **Du, Y**, Dodel, RC., Saura, J., Fishman, CE., DeLong, CA., Piccardo, P, Petegnief, V., Ghetti, B. and Paul SM. Apolipoprotein E is essential for amyloid deposition in the APPV717F transgenic mouse model of Alzheimer's disease. *Proc. Natl. Acad. Sci. USA* 1999 96: 15233-15238.
19. Dodel RC, **Du Y**, Bales KR, Gao F, Eastwood B, Glazier B, Zimmer R, Cordell B, Hake A, Evans R, Gallagher-Thompson D, Thompson LW, Tinklenberg JR, Pfefferbaum A, Sullivan EV, Yesavage J, Alstiel L, Gasser T, Farlow MR, Murphy GM Jr, Paul SM.  $\alpha_2$  Macroglobulin and The Risk of Alzheimer's Disease. *Neurology*. 54:438-442, 2000
20. Dodel RC, Bales KR, Bender M, Nunez G, Hyslop G, Oertel WH, Paul SM, **Du Y** Bcl-2 Protects SK-N-SH Cells from 6-Hydroxydopamine Induced Apoptosis by Inhibition of Cytochrome c Redistribution. (Collins MA, Storch A, Ed.). pp. 219-231 Kluwer Academic; New York, 2000
21. **Du Y**, Dodel RC, Eastwood BJ, Bales KR, Gao F, Lohmuller F, Muller U, Kurz A, Zimmer R, Evans RM, Hake A, Gasser T, Oertel WH, Griffin WS, Paul SM, Farlow MR. Association of an Interleukin 1a Polymorphism and Alzheimer's Disease *Neurology* 2000 55(4):480-3.

22. Bales KR, **Du Y**, Holtzman D, Cordell B, and Paul SM. Neuroinflammation and Alzheimer's disease: critical roles for cytokine/Abeta-induced glial activation, NF-kappaB, and apolipoprotein E. *Neurobiol Aging*. 2000 21(3):427-32
23. Dodel RC, Lohmuller F, **Du Y**, Eastwood B, Gocke P, Oertel WH, Gasser T. A polymorphism in the intronic region of the IL-1alpha gene and the risk for Parkinson's disease. *Neurology* 2001 56(7):982-983.
24. **Du Y**, Dodel R, Hampel H, Buerger K, Lin S, Eastwood B, Bales K, Gao F, Moeller HJ, Oertel W, Farlow M, Paul S. Reduced CSF levels of amyloid  $\beta$ -peptide antibody in Alzheimer's disease. *Neurology* 2001 57(5):801-805
25. **Du, Y**, Ma, M, Lin, SZ, Gao, F., Dodel, RC, Bales, KR, Triarhou, LC, Chernet, E, Perry, K, Nelson, DLG, Luecke, S; Phebus, LA, Bymaster, FP, Paul, SM. Minocycline Prevents Nigrostriatal Dopaminergic Neurodegeneration in the MPTP Model of Parkinson Disease. *Proc. Natl. Acad. Sci. USA* 2001 98: 14669-14674
26. Dodel RC, **Du Y**, Depboylu C, Kurz A, Eastwood B, Farlow M, Oertel WH, Muller U, Riemenschneider M. A Polmorphism in the Cystatin C Promoter Region is not Associated with an Increased Risk of Alzheimer's Disease. *Neurology* 2001, 98: 14669-14674
27. S. Lin, Y. Zhang, R.C. Dodel and **Y. Du**. Minocycline blocks nitric oxide-induced neurotoxicity by inhibition p38 MAP kinase in rat cerebellar granule neurons. *Neurosci. Lett*. 2001, 315(1-2):61-64.
28. F. Gao, K. Bales, R. Dodel, XM Chen, JY Liu, H. Hampel, M. Farlow, SM Paul, **Y. Du**. NF- $\kappa$ B mediates IL-1 $\beta$ -induced synthesis/release of  $\alpha_2$ -macroglobulin in human glial cell line. *Brain Res. Mol. Brain Res*. 2002, 105: 108-114
29. KL Arvin, BH Han, **Y Du**, S. Lin, SM Paul, DM Holtzman. Minocycline Markedly Protect the Neonatal Brain Against Hypoxic-Ischemic Injury. *Ann Neurol* 2002, 52: 54-61
30. R Dodel, H Hampel, C Depboylu, S Lin, F Gao, S Schock, S Jäckel, X Wei, K Buerger, C Höft; B Hemmer, H Möller, M Farlow, WH Oertel, N Sommer, **Y Du**. Human Antibodies Against Amyloid  $\beta$ -peptide, A Potential Treatment For Alzheimer Disease. *Ann Neurol* 2002, 52: 54-61
31. Nessler S, Dodel R, Bittner A, Reuss S, **Du Y**, Hemmer B, Sommer N. Effect of minocycline in experimental autoimmune encephalomyelitis. *Ann Neurol*. 2002 52:689-690.
32. D.K.Lahiri, G.M.Alley, Y.W.Ge, **Y.Du**. Functional characterization of the 5'-regulatory region of the murine apolipoprotein gene. *Ann N Y Acad Sci*. 2002 973:340-344.
33. S. Lin, X. Wei, Y. Xu, C. Yan, R. C. Dodel, Y. Zhang, J. Liu, J. E. Klaunig, M. R. Farlow, **Y. Du**. Minocycline blocks 6-hydroxydopamine -induced neurotoxicity and free radical production in rat cerebellar granule neurons. *Life Sci*. 2003 72:1635-1641
34. C. Depboylu, **Y. Du**, U. Müller, A. Kurz, R. Zimmer, M. Riemenschneider, T. Gasser, W.H. Oertel, R. C. Dodel. Interleukin-10 Promoter Region Polymorphisms and Susceptibility to Alzheimer's Disease. *Neurosci Lett* 2003 342(1-2):132-134.
35. **R.C. Dodel, H. Hampel, Y. Du**. Immunotherapy for Alzheimer's disease. *Lancet Neurol*. 2003 2: 215-220
36. **Y. Du**, X. Wei, R.C. Dodel, N. Sommer, H. Hampel, F. Gao, Z. Ma, L. Zhao, M. R. Farlow. Human Anti-A $\beta$  Antibodies Block A $\beta$  Fibril Formation and Prevent A $\beta$ -induced Neurotoxicity. *Brain* 2003 126: 1935-1939.
37. S. Lin, C. Yan, X. Wei, S. M. Paul, and **Y. Du**. p38 MAP Kinase Mediates Bilirubin-Induced Neuronal Death of Cultured Rat Cerebellar Granule Neurons. *Neurosci Lett*. 2003 353:209-212
38. C. Depboylu, F. Lohmüller, P. Gocke, **Y. Du**, R. Zimmer, W.H. Oertel, T. Gasser, U. Müller, R. C. Dodel. An Interleukin-6 Promoter Variant is not Associated with an Increased Risk for Alzheimer Disease. *Dementia and Geriatric Cognitive Disorders* 2004 17 (3): 170-173

39. H. Hampel, S. J. Teipel, T. Fuchsberger, N. Andreasen, J. Wiltfang, M. Otto, Y. Shen, R. Dodel, **Y. Du**, M. Farlow, H-J. Möller, K. Blennow, .and K. Buerger. Value of CSF b-Amyloid<sub>1-42</sub> and tau as predictors of Alzheimer's disease in patients with mild cognitive impairment. *Molecular Psychiatry*, 2004, 9(7):705-10.
40. J. C. Möller, C. Depboylu, H. Kölsch, F. Lohmüller, O. Bandmann, P. Gocke, **Y. Du**, S. Paus, U. Wüllner, T. Gasser, W. H. Oertel, T. Klockgether, R. C. Dodel. Lack of Association between the Interleukin-1 alpha (-889) Polymorphism and Early-Onset Parkinson's Disease. *Neurosci Lett*. 2004 359:195-197
41. Diguët E, Fernagut PO, Wei X, **Du Y**, Rouland R, Gross C, Bezard E, Tison F. Deleterious effects of minocycline in animal models of Parkinson's disease and Huntington's disease. *Eur J Neurosci*. 2004 19:3266-76.
42. R. C. Dodel, **Y. Du**, C. Depboylu, H. Hampel, L. Frolich, A. Haag, U. Hemmeter, S. Paulsen, S. J. Teipel, S. Brettschneider, H. J. Möller, X. Wei, M. Farlow, N. Sommer, W. H. Oertel. Intravenous immunoglobulins containing antibodies against  $\beta$ -amyloid for the treatment of Alzheimer's disease. *Journal of Neurology, Neurosurgery, and Psychiatry* 2004 75:1472-4
43. X. Wei, L. Zhao, Z. Ma, D. M. Holtzman, C. Yan, R. C. Dodel, H. Hampel, W. Oertel, M. R. Farlow, **Y. Du**. Caffeic Acid Phenethyl Ester Prevents Neonatal Hypoxic-ischemic Brain Injury. *Brain* 2004 127:2629-35
44. S. Brettschneider, N. G. Morgenthaler, S. J. Teipel, C. Fischer-Schulz, K. Bürger, R. Dodel, **Y. Du**, H.-J. Möller, A. Bergmann, H. Hampel. Decreased serum amyloid-b1-42-autoantibody levels in Alzheimer's disease using a newly developed immuno-precipitation assay with radiolabelled amyloid  $\beta$ 1-42 peptide. *Biol. Psychia*. 2005 57:813-6.
45. X. Wei, L. Zhao, J. Liu, R. C. Dodel, M. R. Farlow, **Y. Du**. Minocycline Inhibits p38 MAP Kinase and Caspase 3 Activation and Prevents Gentamicin-Induced Ototoxicity. *Neuroscience* 2005 131:513-21.
46. **Y. Du**, X. Chen, X. Wei, Y. Ge, , K. R. Bales, D. T Berg, , S. M. Paul, M. R. Farlow, and. Debomoy K. Lahiri. NF- $\kappa$ B Mediates Amyloid- $\beta$  Peptide-stimulated Activity of the Human Apolipoprotein E gene promoter in Human Astroglial cells. *Mol Brain Res*. 2005, 136:177-88.
47. Noelker C, Bacher M, Gocke P, Wei X, Klockgether T, **Du Y**, Dodel R. The flavanoide caffeic acid phenethyl ester blocks 6-hydroxydopamine-induced neurotoxicity. *Neurosci Lett*. 2005, 383:39-43
48. Lin S, Wei X, Bales KR, Paul ABC., Ma Z, Yan G, Paul SM, **Du Y**. Minocycline Blocks Bilirubin Neurotoxicity and Prevents Hyperbilirubinemia-Induced Cerebellar Hypoplasia in the Gunn Rat. *Eur J Neurosci*. 2005, 22:21-27
49. Lin S, Tagliabracci VS, Chen X, **Du Y**. Albumin protects cultured cerebellar granule neurons against zinc neurotoxicity. *Neuroreport* 2005, 16:1461-5.
50. Tan J., Ma Z, Han L, Du R, Zhao L, Wei X, Hou D, Johnstone B, Farlow M, **Du Y**. Caffeic Acid Phenethyl Ester (CAPE) Possesses Potent Cardioprotective Effects in a Rabbit Model of Acute Myocardial Ischemia / Reperfusion Injury. *American Journal of Physiology, Heart and Circulatory Physiology* 2005, in press
51. Buerger K, Teipel SJ, Zinkowski R, Sunderland T, Andreasen N, Blennow K, Ewers M, DeBernardis J, Shen Y, Kerkman D, Du Y, Hampel H. Increased levels of CSF phosphorylated tau in apolipoprotein E 4 carriers with mild cognitive impairment. *Neurosci Lett*. 2005, in press

### C. Research Support

#### Ongoing and Complete Research Support:

IIRG-99-1667 Du (PI) R01 AG20248-01A1 Du (PI)

9/1/02 – 8/31/05

NIH/NIA

Interleukin 1 $\alpha$  polymorphism and Alzheimer's disease.

The major goal of this grant is to investigate how IL-1 $\alpha$  polymorphism is involved in the pathogenesis of Alzheimer's disease.

Alzheimer Association

8/1/99 – 7/31/02

The Role of Alpha-2-Macroglobulin in the Pathogenesis of Alzheimer's Disease.

The major goal of this grant is to characterize how a2M is involved in the pathogenesis of Alzheimer's disease.

Du (PI)

10/1/00-9/30/01

Principal Investigator/Program Director (Last, First, Middle): Du, Yansheng

Lilly Center for Women's Health

NF- $\kappa$ B-Mediated Release/Synthesis of Apolipoprotein E and A $\beta$ -induced Neurotoxicity: Regulation by Estradiol 17 $\beta$

The major goal of this grant is to investigate how Estradiol-17 $\beta$  regulate apoE and A $\beta$ -induced neurotoxicity.  
Du (PI) 10/1/99-9/30/00

Lilly Center for Women's Health

Amyloid Precursor Protein Processing, a2Macroglobulin and Apolipoprotein E: Regulation by Estradiol 17 $\beta$  and Selective Estrogen Receptor Modulators (SERMs).

The major goal of this grant is to continue conducting old project and start some new experiments to characterize how Estradiol-17 $\beta$  and SERMS regulate APP processing, apoE, and a2M.

Du (PI) 10/1/98-9/30/99

Lilly Center for Women's Health

APP and ApoE: Regulation by Estradiol-17 $\beta$  and SERMS.

The major goal of this grant is to characterize how Estradiol-17 $\beta$  and SERMS regulate APP processing and apoE.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME <b>Loren J. Field</b>		POSITION TITLE <b>Professor of Medicine and Pediatrics</b>	
eRA COMMONS USER NAME <b>LJFIELD</b>			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
State University of New York at Oswego	B.A.	1978	Biology
State University of New York at Buffalo	M.S.	1980	Cell & Mol. Biol.
State University of New York at Buffalo	Ph.D.	1982	Cell & Mol. Biol.

**NOTE: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.**

**A. Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

THESIS: Field, L.J. (1983). A comparison of ScV-k1 and ScV-k2 dsRNAs: An explanation for viral exclusion. Ph.D. Thesis, State University of New York at Buffalo, submitted September 1982.

**POSTDOCTORAL TRAINING:**

1983: Postdoctoral Associate, Department of Cell and Molecular Biology, SUNY at Buffalo, New York.

1983-1984: N.I.H. Postdoctoral Trainee, and 1985 N.I.H. Postdoctoral Fellow, Department of Molecular Biology, Roswell Park Memorial Institute, Buffalo, New York

**B. Selected peer-reviewed publications (in chronological order).** Do not include publications submitted or in preparation.

3. **Field, LJ**, Bobek, LA, Brennan, VE, Reilly, JD and Bruenn, JA. (1982). There are at least two yeast viral dsRNAs of the same size: An explanation for viral exclusion. *Cell* 31:193-200.

9. **Field, LJ**. (1988). Atrial natriuretic factor-SV40 T antigen transgenes produce tumors and cardiac arrhythmias in mice. *Science* 239:1029-1033.

15. **Field, LJ**. (1991). Cardiovascular research in transgenic animals. *Trends in Cardiovascular Medicine* 1: 141-146.

20. Katz, E, Steinhilper, ME, Daud, A, Delcarpio, JB, Claycomb, WC and **Field, LJ**. (1992) Cardiomyocyte proliferation in mice expressing a-cardiac myosin heavy chain-SV40 T antigen transgenes. *Am J Physiol* 262:H1867-1876.

25. Jones, LR and **Field, LJ**. (1993) Residues 2-25 of phospholamban are insufficient to inhibit the Ca<sup>++</sup> transport ATPase of cardiac sarcoplasmic reticulum. *J Biol Chem* 268:11486-11488.

32. Soonpaa, MH, Koh, GY, Klug, MG and **Field, LJ**. (1994) Formation of nascent intercalated discs between grafted fetal cardiomyocytes and host myocardium. *Science* 264:98-101.

33. Kim, KK, Soonpaa, MH, Daud, AI, Kim, JS, Koh, GY and **Field, LJ**. (1994). Tumor suppressor gene expression during normal and pathologic myocardial growth. *J Biol Chem* 269:22607-22613.

38. Koh, GY, Kim, SJ, Klug, MG, Park, K, Soonpaa, MH and **Field, LJ**. (1995) Targeted expression of TGF- $\beta$ 1 and neovascularization in hearts bearing intracardiac grafts. *J Clin Invest* 95:114-121.

42. Koh, GY, Soonpaa, MH, Klug, MG, Pride, HP, Zipes, DP, Cooper, BJ and **Field, LJ**. (1995) Stable fetal cardiomyocyte grafts in the hearts of dystrophic mice and dogs. *J Clin Invest* 96:2034-2042.

45. Klug, MG, Soonpaa, MH, Koh, GY and **Field, LJ**. (1996) Genetically selected cardiomyocytes from differentiating embryonic stem cells form stable intracardiac grafts. *J Clin Invest* 98:216-224.

46. Kim, KK, Daud, AI, Wong, SC, Pajak, L, Tsai, S-C, Wang, H, Henzel, WJ and **Field, LJ.** (1996) Mouse RAD50 has limited epitopic homology to p53 and is expressed in the adult myocardium. *J Biol Chem* 271:29255-29264.
47. Sutton, J, Costa, R, Klug, M, **Field, LJ.**, Xu, D, Largaespada, DA, Fletcher, CF, Jenkins, NA, Copeland, NG, Klemsz, M and Hromas, R. (1996) Genesis, a winged helix transcriptional repressor with expression restricted to embryonic stem cells. *J Biol Chem* 271:23126-23133.
50. Soonpaa, MH, Koh, GY, Pajak, L, Jing, S, Wang, H, Franklin, M, Kim, KK and **Field, LJ.** (1997) Cyclin D1 over-expression promotes cardiomyocyte DNA synthesis and multinucleation in transgenic mice. *J Clin Invest* 99:2644-2654.
52. Soonpaa, MH and **Field, LJ.** (1998) A survey of studies examining mammalian cardiomyocyte DNA synthesis. *Circ Res* 83:15-26.
55. Tsai, S-C, Pasumarti, K, Pajak, L, Franklin, M, Patton, B, Henzel WJ, and **Field, LJ.** (2000) SV40 Large T Antigen binds a novel BH3 containing pro-apoptosis protein in the cytoplasm. *J Biol Chem* 275:3239-3246.
56. Nakajima, H, Nakajima, HO, Salcher, O, Dittiè, AS, Dembowsky, K, Jing, S and **Field, LJ.** (2000) Atrial, but not ventricular, fibrosis in mice expressing a mutant TGF- $\beta$ 1 transgene in the heart. *Circ Res* 86:571-579.
57. Pasumarthi, KBS, Nakajima, H, Nakajima, HO, Jing, S, **Field, LJ.** (2000) Enhanced cardiomyocyte DNA synthesis during myocardial hypertrophy in mice expressing a modified TSC2 transgene. *Circ Res* 86: 1069 - 1077.
58. Reinlib, L and **Field, LJ.** (2000) Transplantation: Future Therapy for Cardiovascular Disease? An NHLBI Workshop. *Circulation* 101:e182-e187.
59. Huh, NE, Pasumarthi, KBS, Soonpaa, MH, Jing, S, Patton, B and **Field, LJ.** (2001) Functional abrogation of p53 is required for T-Ag induced proliferation in cardiomyocytes. *J Mol Cell Cardiol* 33:1405-1419.
60. Pasumarthi, KBS, Tsai, S-C, **Field, LJ.** (2001) Co-expression of mutant p53 and p193 render embryonic stem cell-derived cardiomyocytes responsive to the growth-promoting activities of adenoviral E1A. *Circ Res* 88:1004-1011.
61. Zandstra, PW, Bauwens, C, Yin, T, Liu, Q, Schiller, H, Zweigerdt, R, Pasumarthi KBS, and **Field, LJ.** (2003) Scalable production of embryonic stem cell-derived cardiomyocytes. *Tissue Engineering* 9:767-98.
62. Rubart, M, Wang, E, Dunn, KW and **Field, LJ.** (2003) Two photon molecular excitation imaging of Ca<sup>2+</sup> transients in Langendorff-perfused mouse hearts. *Am J Physiol* 284:C1645-C1688.
63. Rubart, M, Pasumarthi, KBS, Nakajima, H, Soonpaa, M, Nakajima, HO and **Field, LJ.** (2003) Physiologic coupling of donor and host cardiomyocytes following cellular transplantation. *Circ Res* 92:1217-1224.
64. Murry, CE, Soonpaa, MH, Reinecke, H, Nakajima, H, Nakajima, HO, Rubart, M, Pasumarthi, KBS, Virag, JI, Bartelmez, JH, Poppa, V, Bradford, G, Dowell, JD, Williams, DA and **Field, LJ.** (2004) Absence of Cardiac Transdifferentiation after Direct Injection of Adult Hematopoietic Stem Cells into Myocardial Infarcts. *Nature* 428:664-668.
65. Verheule, S., Sato, T., Everett IV, T., Engle, S.K., Otten, K., Rubart, M., Nakajima, H.O., Nakajima, H., **Field, L.J.** and Olgin, J.E. (2004) Increased Vulnerability to Atrial Fibrillation in Transgenic Mice with Selective Atrial Fibrosis Due to Overexpression of TGFB-1. *Circ Res* 94:1458-1465.
66. Nakajima, H., Nakajima, H.O., Tsai, S.-C. and **Field, L.J.** (2004) Expression of mutant p193 and p53 permits cardiomyocyte cell cycle reactivation following myocardial infarction in transgenic mice. *Circ Res* 94, 1606-1614.
67. Rubart, M., Soonpaa, M.H., Nakajima, H. and **Field, L.J.** (2004) Spontaneous and Evoked Intracellular Calcium Transients in Donor-Derived Myocytes Following Intra-cardiac Myoblast Transplantation. *J Clin Invest* 114:775-783.
68. Pasumarthi, K.B.S., Nakajima, H., Nakajima, H.O., Soonpaa, M.H. and **Field, L.J.** (2005) Targeted expression of cyclin D2 results in cardiomyocyte cell cycle activation and concomitant regression of myocardial infarct size in transgenic mice. *Circ Res* 96:110-118.
69. Murry, C.E., **Field, L.J.** and Menasché, P. Cell-Based Cardiac Repair Reflections at the 10-Year Point. *Circulation*, in press.
70. Schroeder, M., Willbold, E., Burg, M., Ruediger, M., **Field, L.J.**, Niebruegge, S., Lehmann, J. and Zweigerdt, R. Embryonic Stem Cell Differentiation and Lineage Selection in a Stirred Bench Scale Bioreactor with Automated Process Control. *Biotechnology and Bioengineering*, in press.
71. Nakajima, H., Nakajima, H.O., Dembowsky, K. and **Field, L.J.** Cardiomyocyte cell cycle activation ameliorates fibrosis in the atrium. *Circ Res*, under revision.

**C. Research Support.** List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

(1)

1. Source of Support: N.I.H., National Heart Lung and Blood Institute
2. Identification #: 1 RO1 HL45453
3. Project Title: Cloning genes that regulate myocardiocyte proliferation.
4. Principal Investigator: Loren J. Field
5. Project Period: 7/90-3/07
6. Description: This grant is concerned with identifying genes that regulate cardiomyocyte cell cycle using an SV40 transgenic mouse model for gene discovery.

(2)

1. Source of Support: N.I.H., National Heart Lung and Blood Institute
2. Identification #: 1 RO1 HL69119
3. Project Title: Bone marrow stem cells and cardiac repair
4. Principal Investigator: Loren J. Field
5. Project Period: 9/01-9/05
6. Description: This grant is concerned with comparing the cardiomyogenic potential of a number of different bone marrow stem cells to embryonic stem cells following in vitro differentiation and following transplantation into the heart.

(3)

1. Source of Support: N.I.H.
2. Identification #: 1 R01 HL75609
3. Project Title: Cyclin D2 and cardiac regeneration
4. Principal Investigator: Loren J. Field
5. Project Period: 12/03-11/07
6. Description: This grant is concerned with examining the degree to which forced expression of cyclin D2 can effect regenerative growth post MI.

(4)

1. Source of Support: N.I.H.
2. Identification #: 1 P30 CA82709
3. Project Title: Cancer Center Support Grant
4. Principal Investigator: Stephen Williams
  - a. Transgenic and Knock-out Mouse Core; Loren J. Field, P.I.
5. Project Period: 9/99-6/04
7. Description: This grant provides funds to defray the costs of generating transgenic and knock-out mice for members of the Indiana University Cancer Center.

Principal Investigator/Program Director (Last, First, Middle):

## BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME <b>Fife, Rose S, M.D.</b>		POSITION TITLE Barbara F. Kampen Professor of Women's Health Professor of Medicine and Biochemistry and Molecular Biology Associate Dean for Research	
eRA COMMONS USER NAME rfife			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Barnard College, New York, NY	B.A.	1971	Biology
Johns Hopkins University School of Medicine, Baltimore MD	M.D.	1975	Medicine
Rollins School of Public Health, Emory University, Atlanta, GA	M.P.H.	2006 (anticipated)	Public Health

**NOTE: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.**

**A. Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

- 1975 - 1978 Residency in Internal Medicine, Johns Hopkins University School of Medicine, Baltimore, MD
- 1978 - 1979 Fellowship in Gastroenterology, University of Maryland School of Medicine, Baltimore, MD
- 1979 - 1981 Senior Fellowship in Rheumatology, University of Washington School of Medicine, Seattle, WA
- 1981 - 1986 Assistant Professor of Medicine, Indiana University School of Medicine, Indianapolis, IN
- 1981-Present Attending Physician, Indiana University Hospital, Wishard Memorial Hospital, Richard L Roudebush Veterans Administration Hospital
- 1984 - 1992 Chief of Rheumatology, Wishard Memorial Hospital
- 1986 - 1993 Associate Professor of Medicine and Biochemistry and Molecular Biology, Indiana University School of Medicine
- 1989-Present Member, Graduate Faculties, Indiana University
- 1990-2001 Assistant Dean for Research, Indiana University School of Medicine
- 1993-Present Professor of Medicine and Biochemistry and Molecular Biology, Indiana University School of Medicine
- 1997-Present Director, Indiana University National Center of Excellence in Women's Health
- 2001–Present Barbara F. Kampen Professor of Women's Health, Indiana University School of Medicine
- 2001-Present Associate Dean for Research, Indiana University School of Medicine

### **Other Experience and Professional Memberships**

Fellow, American College of Physicians; Fellow, American College of Rheumatology; President-Elect, Central Society for Clinical Research; Member, American Society for Biochemistry and Molecular Biology; Member, American Society for Cell Biology; Member, American Association for Cancer Research; Member, Society for Women's Health Research Member, American Medical Women's Association; Member, Editorial Advisory Board, Med Crossfire, J Women's Health and Gender-Related Medicine; Associate Editor, J Lab Clin Med

**Patent:** "Novel Cancer Treatment Using Tetracyclines," patent number 08/431,751, 1997

### **Honors:**

1970	Phi Beta Kappa, Barnard College
1971	Magna cum laude, Barnard College
1991	Alpha Omega Alpha
1986 - 1989	Allied Corporation Investigator in Osteoarthritis, Arthritis Foundation
1992 - 1996	Member, National Advisory Council on Nursing Research, NINR, NIH
1997 - 2001	Member, GCRC Study Section, NCCR, NIH
2001 - 2004	Member, Susan G. Komen Breast Cancer Fund Grant Review Subcommittee

### **B. Selected peer-reviewed publications (in chronological order).**

1. **Fife RS**, Sledge G, Roth B, Proctor C. Effects of doxycycline on human prostate cancer cells *in vitro*. Cancer Lett 127:37-41, 1998
2. **Fife RS**, Sledge GW. Effects of doxycycline in cancer cells. Adv Dent Res 12:94-96, 1998
3. **Fife RS**, Sledge G, Sissons S, Zerler B. Effects of tetracyclines on angiogenesis *in vitro*. Cancer Lett 153:75-78, 2000
4. **Fife RS**, Moskovic C, Dynak H, Winner C, Vahratian A, Laya M, Jameson L, Paskett E. Development and implementation of novel community outreach methods in women's health issues. J Women's Health and Gender-Related Medicine 10:27-37, 2001
5. Weiner C, Frid D, Droker M, **Fife RS**. Leveraging healthcare for the greater good. J Women's Health and Gender-Related Medicine 10:533-539, 2001
6. Moreland L, Gugliotti R, King K, Chase M, Greco T, **Fife R**, Korn J, Tesser J, Caldwell J, Schnitzer T, Lyons D, Schwertschlag U. Results of a Phase I/II randomized, masked, placebo controlled trial of recombinant human interleukin 11 (rhIL-11) in the treatment of subjects with active rheumatoid arthritis. Arthritis Res 3:349-351, 2001
7. Petrone D, Condemi J, **Fife R**, Gluck O, Cohen S, Dalgin P. A double-blind, randomized, placebo-controlled trial in Sjogren's Syndrome patients with xerostomia and keratoconjunctivitis sicca. Arthritis Rheum 46:748-754, 2002
8. **Fife RS**, Chase W, Dore R, Weisenhutter C, Lockhart P, Tindall E, Suen J. Civemline: An effective and safe agent for the treatment of xerostomia in patients with Sjogren's Syndrome. Arch Int Med 162:1293-1300, 2002
9. Toi M, Bando H, Imai A, Ramachandran C, Melnick SJ, **Fife RS**, Carr RE, Neeman I, Kaplan B, Lansky EP. Pomegranate extracts inhibit both induction of angiogenic molecules from tumor cells and endothelial cell growth directly. Angiogenesis, 2003
10. **Fife RS**. Development of a comprehensive women's health program in an academic medical center. J Women's Health 12:869-878, 2003
11. **Fife RS**, Stott B, Carr RE. Effects of a selective cyclooxygenase-2 inhibitor on cancer cells *in vitro*. Cancer Biol Ther (3 :228-232), 2004
12. **Fife RS**, P Keener, EM Meslin, M Randall, RL Schiffmiller. Faculty Ownership of Medical Facilities: Inappropriate Conflict or an Opportunity that Benefits Physicians and Patients? Acad Med 79: 1051-1055, 2004

### C. Ongoing Research Support

282-97-0075	Fife, Rose S. (PI)	9/30/97-9/30/06
Department of Health and Human Services National Center of Excellence in Women's Health The major goal of this project is to establish model of women's health including clinical care, research mentoring, education leadership, and community outreach.		
1 C06 RR15481-01	Fife, Rose S. (PI)	3/15/01-10/30/05
National Institutes of Health-National Center for Research Resources Construction of Neuroscience Facility at Indiana University School of Medicine		
G20 RR016995-01A1	Fife, Rose S. (PI)	2/1/03-1/31/06
National Institutes of Health Animal Facilities Improvement Grant Construction grant		
1 C76 HF 00742-01-00	Fife, Rose S. (PI)	9/1/03-9/30/06
Health Resources and Services Administration Health Care and Other Facilities: Indiana University Center for Bone Cancer Research		
1 R21 AR50678-01	Fife, Rose S. (PI)	9/26/03-6/30/05
National Institutes of Health Nitric oxide and cyclooxygenase in arthritis Study of interactions between nitric oxide synthase and cyclooxygenase in an animal model of inflammatory arthritis.		
CH11233	Fife, Rose S. (PI)	3/15/04-3/14/2006
Department of Energy Indiana University School of Medicine Medical Information Sciences Building The major goal of this project is the construction of a new facility for medical research.		
Merck Foundation	Fife, Rose S. (PI)	01/01/04-12/31/06
Educational Outreach for Hispanic Women in Indianapolis		
Nina Mason Pulliam Charitable Trust	Fife, Rose S. (PI)	3/22/04-4/17/06
Health Education for Hispanic Women in Indianapolis		
Johnson & Johnson Grant Program	Fife, Rose, S. (PI)	7/01/04-6/30/06
Outreach to Hispanic Women in Indianapolis		
C06 RR020128-01	Fife, Rose S. (PI)	9/24/04-9/30/07
National Institutes of Health Build Out of Shell Space for Medical Genetics Core Facilities Construction grant		
HHSP233200400852P	Fife, Rose S. (PI)	9/30/04 09/29/05
Department of Health and Human Services The National Centers of Excellence in Women's Health and the National Community Centers in Women's Health Prevention Projects on Diabetes/Obesity or Cancer		

HHSP233200400934P Fife, Rose S. (PI) 09/30/04-12/31/06  
Department of Health and Human Services  
Indiana University National Center of Excellence in Women's Health Heart Truth Professional  
Education Program

1 T35 AG024057-01A1 Fife, Rose S. (PI) 05/01/05-04/30/10  
National Institutes of Health  
Short-Term Training Grant in Women's Health

### **Completed Research**

1 G20 RR14015-01 Fife, Rose S. (PI) 6/1/99-5/31/03  
National Institutes of Health-National Center for Research Resources  
Animal Facilities Improvement Grant  
The major goals of this project are developing and improving the institutional animal resource  
facility.

CollaGenex Fife, Rose S. (PI) 9/17/99-6/30/03  
Effects of COL-3 on Human Breast Adenocarcinoma *In Vitro* and in a Mouse Model  
Study of Chemically Modified Tetracyclines in Cancer.

IR03CA92745-01 Fife, Rose S. (PI) 7/1/01-6/30/03  
National Institutes of Health  
Role of Nitric Oxide in the Progression of Murine Mammary Cancers  
Study of effect of nitric oxide on tumor aggressiveness.

1 C76 HF 00525 01 Fife, Rose S. (PI) 9/15/02-9/15/04  
Health Resources and Services Administration  
Indiana Genomics Initiative Animal Facilities Construction

RFQ 02T020146 Fife, Rose S. (PI) 9/30/02-9/30/03  
Department of Health and Human Services  
Outreach and Education on Domestic Violence in Rural Settings  
Collaborative project with Drexel CoE and Vermont CCoE

RFQ 02T0200814 Fife, Rose S. (PI) 9/30/02-6/30/04  
Department of Health and Human Services  
Professional Service – CDC's DES Update: Implementation Activities by the National Centers of  
Excellence in Women's Health Educational outreach about DES.

04-RQ-32122 Fife, Rose S. (PI) 5/1/2004-4/30/2005  
US Department of the Interior  
Educational Seminars Promoting Organ and Tissue Donation  
To create a PowerPoint presentation and written material for three live presentations promoting  
organ and tissue donation.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Shao-Ling Fong	POSITION TITLE		
eRA COMMONS USER NAME	Associate Professor		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Chung-Hsing University, Taiwan	B.S.	1966	Agriculture Chemistry
Southern Illinois University	M.S.	1974	Physical Chemistry
Southern Illinois University	PH.D.	1978	Biochemistry

**A. Positions and Honors.**

1977-1979: Research Associate, Baylor College of Medicine  
 1979-1980: Research Instructor, Baylor College of Medicine  
 1980-1987: Research Assistant Professor, Baylor College of Medicine  
 1987-1989: Associate Research Scientist, Purdue University  
 1989-1995: Assistant Professor, Indiana University  
 1995-present: Associate Professor, Graduate School Faculty, Indiana University

**B. Selected Peer-reviewed publications (inchronological order).**

- Bridges, C.D.B. and Fong, S.-L. Different distribution of receptors for peanut and ricin agglutinins between inner and outer segments of rod cells. *Nature* 282:513-515 (1979).
- Bridges, C.D.B., Fong, S.-L., and Alvarez, R.A. Separation by programmed-gradient hplc of vitamin A isomers, their esters, aldehydes, oximes and vitamin A2: Presence of retinyl ester in dark-adapted goldfish pigment epithelium. *Vision Res.*, 20:355-360 (1980).
- Bridges, C.D.B. and Fong, S.-L. Lectins as probes of glycoprotein and glycolipid oligosaccharides in rods and cones. *Neurochemistry* 1:255-267 (1980).
- Hargrave, P.A., Fong, S.-L., McDowell, J.H., Mas, M.T., Curtis, D.R., Wang, J.K., Juszczak, E., and Smith, D.P. The partial primary structure of bovine rhodopsin and its topography in the retinal rod cell disc membrane. *Neurochemistry* 1:231 (1980).
- Bridges, C.D.B. and Fong, S.-L. Lectin receptors on rod and cone membranes. *Photochem. Photobiol.*, 32:481-486 (1980).
- Alvarez, R.A., Bridges, C.D.B., and Fong, S.-L. High-pressure liquid chromatography of fatty acid esters of retinol isomers -- analysis of retinyl esters stored in the eye. *Invest. Ophthalm. & Vis. Sci.*, 20:304-313 (1981).
- Liou, G.I., Fong, S.-L., and Bridges, C.D.B. Comparison of cytosol retinol binding proteins from bovine retina, dog liver and rat liver. *J. Biol. Chem.*, 256:3153-3155 (1981).
- Bridges, C.D.B., Alvarez, R.A., and Fong, S.-L. Vitamin A in human eyes - amount, distribution and composition. *Invest. Ophthalm. & Vis. Sci.*, 22:706-714 (1982).
- Liou, G.I., Bridges, C.D.B., Fong, S.-L., Alvarez, R.A., and Gonzalez-Fernandez, F. Vitamin A transport between retina and pigment epithelium - an interstitial protein carrying endogenous retinol (interstitial retinol-binding protein). *Vision Res.*, 22:1457-1467 (1982).
- Hargrave, P.A., McDowell, J.H., Siemiatkowski-Juszczak, E.C., Fong, S.-L., Kuhn, H., Wang, J.K., Curtis, D.R., Mohana Rao, J.K., Argos, P., and Feldmann, R.J. The carboxyl-terminal one-third of bovine rhodopsin: Its structure and function. *Vision Res.*, 22:1429-1438 (1982).
- Fong, S.-L., Tsin, A.T.C., Bridges, C.D.B., and Liou, G.I. "Detergents for Extraction of Visual Pigments--Types, Solubilization and Stability." In *Biomembranes: Visual Pigments and Purple Membranes*. Ed. by L. Packer. *Methods in Enzymology* (eds. Colowick and Kaplan). Academic Press, New York. Vol. 81, Part H, pp. 133-140 (1982).
- Fong, S.-L., Bridges, C.D.B., and Alvarez, R.A. Utilization of exogenous retinol by frog pigment epithelium. *Vision Res.*, 23:47-52 (1983).

13. Hargrave, P.A., McDowell, J.H., Curtis, D.R., Wang, J.K., Juszczak, E., Fong, S.-L., Rao, J.K.M., and Argos, P. The structure of bovine rhodopsin. *Biophys. Struct. Mech.*, 9:235-244 (1983).
14. Fong, S.-L., Liou, G.I., Landers, R.A., Alvarez, R.A., Gonzalez-Fernandez, F., Glazebrook, P.A., Lam, D.M.K., and Bridges, C.D.B. The characterization, localization and biosynthesis of interstitial retinol-binding protein in the human retina. *J.Neurochem.*, 42:1667-1676 (1984).
15. Fong, S.-L., Liou, G.I., Landers, R.A., Alvarez, R.A., and Bridges, C.D.B. Purification and characterization of a retinol-binding glycoprotein synthesized and secreted by bovine neural retina. *J.Biol. Chem.*, 259:6534-6542 (1984).
16. Bridges, C.D.B., Alvarez, R.A., Fong, S.-L., Gonzalez-Fernandez, F., Lam, D.M.K., and Liou, G.I. Visual cycle in the mammalian eye: Retinoid-binding proteins and the distribution of 11-cis retinoids. *Vision Res.*, 24:1581-1594 (1984).
17. Tsin, A.T.C., Alvarez, R.A., Fong, S.-L., and Bridges, C.D.B. Use of high-performance liquid chromatography in the analysis of retinyl and 3,4-didehydroretinyl compounds in tissue extracts of bullfrog tadpoles and goldfish. *Vision Res.*, 24:1835-1840 (1984).
18. Gonzalez-Fernandez, F., Landers, R.A., Glazebrook, P.A., Fong, S.-L., Liou, G.I., Lam, D.M.K., and Bridges, C.D.B. An extracellular retinol-binding glycoprotein in the eyes of mutant rats with retinal dystrophy - development, localization and biosynthesis. *J. Cell. Biol.*, 99:2092-2098 (1984).
19. Hollyfield, J.G., Fliesler, S.J., Rayborn, M.E., Fong, S.-L., Landers, R.A., and Bridges, C.D.B. Synthesis and secretion of interstitial retinol-binding protein by the human retina. *Invest. Ophthalm. & Vis. Sci.*, 26:58-67 (1985).
20. Gonzalez-Fernandez, F., Landers, R.A., Glazebrook, P.A., Fong, S.-L., Liou, G.I., Lam, D.M.K., and Bridges, C.D.B. An extracellular retinol-binding glycoprotein in the rat eye--characterization, localization and biosynthesis. *Neurochem. Int.*, 7:533-540 (1985).
21. Tsin, A.T.C., Alvarez, R.A., Fong, S.-L., and Bridges, C.D.B. Conversion of retinol to 3,4-didehydroretinol in the tadpole. *Comp. Biochem. and Physiol.*, 81B:415-421(1985).
22. Bridges, C.D.B., O'Gorman, S., Fong, S.-L., Alvarez, R.A., and Berson, E. Vitamin A and interstitial retinol-binding protein an eye with recessive retinitis pigmentosa. *Invest. Ophthalm. & Vis. Sci.*, 26:684-691 (1985).
23. Fong, S.-L., Landers, R.A., and Bridges, C.D.B. Varieties of rhodopsin in frog rod outer segment membranes: analysis by isoelectric focusing. *Vision Res.*, 25:1387-1398 (1985).
24. Bridges, C.D.B., Fong, S.-L., Landers, R.A., Liou, G.I., and Font, R.L. Interstitial retinol-binding protein (IRBP) in retinoblastoma. *Neurochem. Int.*, 7:875-881 (1985).
25. Gonzalez-Fernandez, F., Fong, S.-L., Liou, G.I., and Bridges, C.D.B. Interstitial retinol-binding protein (IRBP) in the RCS rat - effect of dark-rearing. *Invest. Ophthalm. & Vis. Sci.*, 26:1381-1385 (1985).
26. Bridges, C.D.B., Oka, M.S., Fong, S.-L., Liou, G.I., and Alvarez, R.A., Retinoid-binding proteins and retinol esterification in cultured retinal pigment epithelium cells. *Neurochem. Int.*, 8:527-534 (1986).
27. Schneider, B.G., Papermaster, D.S., Liou, G.I., Fong, S.-L., and Bridges, C.D.B. Electron microscopic immunocytochemistry of interstitial retinol-binding protein invertebrate retinas. *Invest. Ophthalm. & Vis. Sci.*, 27:679-688 (1986).
28. Bridges, C.D.B., Price, J., Landers, R.A., Fong, S.-L., Liou, G.I., Hong, B.-S., and Tsin, A.T.C. Interstitial retinol-binding protein (IRBP) in subretinal fluid. *Invest. Ophthalm. & Vis. Sci.*, 27:1027-1030 (1986).
29. Liou, G.I., Fong, S.-L., Beattie, W.G., Leone, J., Landers, R.A., Alvarez, R.A., Wang, C., Li, Y., and Bridges, C.D.B. Bovine interstitial retinol-binding protein (IRBP) - isolation and sequence analysis of cDNA clones, characterization and in vitro translation of mRNA. *Vision Res.*, 26:1645-1654 (1986).
30. Carter-Dawson, L., Alvarez, R.A., Fong, S.-L., Liou, G.I., Sperling, H.G., and Bridges, C.D.B. Rhodopsin, 11-cis vitamin A and interstitial retinol-binding protein (IRBP) during retinal development in normal and rd mutant mice. *Developmental Biol.*, 116:431-438 (1986).
31. Bridges, C.D.B., Liou, G.I., Alvarez, R.A., Landers, R.A., Landry Jr., A.M., and Fong, S.-L. Distribution of interstitial retinol-binding protein (IRBP) in the vertebrates. *J. Exp. Zool.*, 239:335-346 (1986).
32. Fong, S.-L., Cook, R.G., Alvarez, R.A., Liou, G.I., Landers, and Bridges, C.D.B. N-terminal sequence homologies in interstitial retinol-binding proteins from 10 vertebrate species. *FEBS Letters*, 205:309-312 (1986).
33. Bridges, C.D.B., Peters Jr., T., Smith, John Edgar, Goodman, DeWitt S., Fong, S.-L., Griswold, M.D., and Musto, N.A. Biosynthesis and secretion of transport proteins - interstitial and serum retinol-binding proteins, transthyretin, transferrin, serum albumin and extracellular sex steroid binding proteins. *Fed. Proc.*, 45:2291-2303 (1986).
34. Bridges, C.D.B., Alvarez, R.A., Fong, S.-L., Liou, G.I., and Ulshafer, R.J. Rhodopsin, vitamin A and interstitial retinol-binding protein in the rd chicken. *Invest. Ophthalm. & Vis. Sci.*, 28:613-617 (1987).
35. Liou, G.I., Li, Y., Wang, C., Fong, S.-L., Bhattacharya, S., and Bridges, C.D.B. Bgl II RFLP recognized by a human IRBP cDNA localized to chromosome 10. *Nucleic Acids Research*, 15:1396 (1987).

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37. Alvarez RA, Liou GI, Fong S-L and Bridges CDB. Levels of alpha- and gamma-tocopherol in human eyes: evaluation of the possible role of IRBP in intraocular alpha-tocopherol transport. *Amer. J. Clin. Nutr.* 46: 481-487 (1987).
38. Bridges CDB, Foster RG, Landers RA and Fong S-L. Interstitial retinol-binding protein and cellular retinal-binding protein in the mammalian pineal. *Vision Res.* 27:2049-2060 (1987).
39. Mathew CGP, Chin KS, Easton DF, Thorpe K, Carter C, Liou GI, Fong S-L, Bridges CDB, Haak H, Nieuwenhuijzen Kruseman AC, Schifter S, Hansen H, Telenius H, Telenius-Berg M and Ponder BAJ. A linked genetic marker for multiple endocrine neoplasia type 2a on chromosome 10. *Nature* 328:527-528 (1987).
40. Fong S-L, Lee PG, Ozaki K, Hara R, Hara T and Bridges CDB. IRBP-like proteins in the eyes of six cephalopod species - immunochemical relationship to vertebrate interstitial retinol-binding protein. *Vision Res.*, 28:563-574 (1988).
41. Fong S-L, Balakier H, Canton H, Bridges CDB and Gallie B. Retinoid-binding proteins in retinoblastoma tumors. *Cancer Res.*, 48:1124-1128 (1988).
42. Chin KS, Mathew CGP, Fong S-L, Bridges CDB, and Ponder BAJ. Sty 1 RFLP recognized by a human IRBP cDNA localized to chromosome 10. *Nucleic Acids Research* 16:1645 (1988).
43. Fong S-L, and Bridges CDB. Internal quadruplication in the structure of human interstitial retinol-binding protein deduced from its cloned cDNA. *J. Biol. Chem.*, 263:15330-15334 (1988).
44. Donoso, L.A., Merryman, C.F., Sery, T.W., Vrabec, T., Arbizu, V., and Fong, S.-L. Human IRBP: Characterization of uveitopathogenic sites. *Current Eye Res.*, 7:1087-1095 (1988).
45. Lin Z-S, Fong S-L and Bridges CDB. Retinoids bound to interstitial retinol-binding protein during light and dark-adaptation. *Vision Res.*, 29:1699-1709 (1989).
46. Donoso LA, Merryman CF, Sery TW, Sanders R, Vrabec T and Fong S-L. Human interstitial retinol binding protein (IRBP): A potent uveitopathogenic autoimmune uveitis (EAU). *J. Immunology* 143:79-83
47. Fong S-L, Fong W-B, Morris AT, Kedzie KM and Bridges CDB. Characterization and comparative structural features of the gene for human interstitial retinol-binding protein. *J. Biol. Chem.*, 265:3648-3653 (1990).
48. Donoso LA, Rodrigues M., Vrabec T.R., Sery T.W., and Fong S-L. IRBP: preparation and characterization of site-specific monoclonal antibodies. *Current Eye Res.* 9: 357-362(1990).
49. Fong S.-L., Fong W.-B., Morris T.A., Kedzie K.M. and Bridges CDB. Characterization and comparative structural features of the gene for human interstitial retinol-binding protein. *J. Biol. Chem.* 265:3648-3653 (1990)
50. Rao NA, Fong S-L, Chen F, Linker-Israeli M and Steinman L. Antigen-specific suppressor cells in experimental autoimmune uveitis, *Ophthalmic Res.* 24:92-98 (1992)
51. Fong S-L. Characterization of the human rod transducin alpha-subunit gene. *Nucleic Acids Res.* 20:2865-2870 (1992)
52. Morris T.A. and Fong S.-L. Characterization of the Gene Encoding Human Cone Transducin Alpha-Subunit (GNAT2). *Genomics* 17:442-448 (1993)
53. Magovcevic I, Weremowicz S, Morton CC, Fong S-L, Berson EL and Dryja TP. Mapping of the human cone transducin alpha-Subunit (GNAT2) gene to 1p13 and mutation analysis in patients with Stargardt's disease, *Genomics* 25, 288-290 (1995)
54. Morris TA and Fong S-L. Localization of upstream silencers involved in the expression of cone transducin alpha-subunit (GNAT2), *Invest. Ophthalm. & Vis. Sci.* 38:196-206 (1997)
55. Ying S, S-L Fong, W-B Fong, Kao CWC, Converse RL and Kao WW-Y. A CAT reporter construct containing 277 bp GNAT2 promoter and 214 bp IRBP enhancer is specifically expressed by cone photoreceptor cells in transgenic mice, *Curr. Eye Res.* 17:777-782 (1998)
56. Fong S-L and Fong W-B. Elements regulating the transcription of human interstitial retinoid-binding protein (IRBP) in cultured retinoblastoma cells, *Curr. Eye Res.*, 18:283-291 (1999)
57. Ying S, Jansen HT, Lehman MN, Fong S-L and Kao WW-Y. Retinal degeneration in cone photoreceptor cell-ablated transgenic mice. *Molecular Vision* 6:101-108 (2000).
58. Fong S-L, Criswell MH, Belecky-Adams T, Fong W-B, McClintick JN, Kao WW-Y, and Edenberg H. Characterization of a transgenic mouse line lacking photoreceptor cell development within the ventral retina. *Exp. Eye Res.* In Press

### C. Research Support.

"Postnatal Development of Mouse Photoreceptors" is a new project. The PI's laboratory has not been supported for the past 3 years. The long term goals of this project are to profile genes that are associated with photoreceptor development and to identify genes that are essential for the development of photoreceptors in transgenic dorsal and ventral retinas.

**BIOGRAPHICAL SKETCH**Provide the following information for the Principal Investigator. **DO NOT EXCEED TWO PAGES.**

NAME Seiji Fukuda	POSITION TITLE Assistant Research Professor, Dept of Microbiology and Immunology Associate Member of IUCC		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Gifu University, School of Medicine, Japan	M.D.	1988	Medicine
Gifu University, School of Medicine, Japan	Resident	1988-1989	Pediatrics
Gifu University, School of Medicine	Ph.D.	1993	Molecular Genetics
Gifu University, School of Medicine	Resident	1993-1995	Pediatrics
Indiana University, School of Medicine	Postdoctoral	1998-2004	Exp. Hematology

**A. Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors.

Include present membership on any Federal Government public advisory committee.

- 06/88-05/89: Resident, Department of Pediatrics, Gifu University School of Medicine, Gifu, Japan  
05/89-01/93: Graduate Student, Department of Pediatrics, Gifu University School of Medicine, Gifu, Japan  
02/93-04/95: Resident, Department of Pediatrics, Gifu University School of Medicine, Gifu, Japan  
04/95-03/97: Instructor: Department of Pediatrics, Gifu University School of Medicine, Gifu, Japan  
04/97-09/97: Chief physician: Department of Neonatology, Gifu Prefecture Hospital, Gifu, Japan  
10/97-12/97: Instructor: Department of Pediatrics, Gifu University School of Medicine, Gifu, Japan  
01/98-06/04: Postdoctoral fellow: Department of Microbiology/Immunology, Indiana University, School of Medicine, IN  
07/04-12/04: Assistant Scientist: Department of Microbiology/Immunology, Indiana University, School of Medicine, IN  
01/05-present Assistant Research Professor, Department of Microbiology/Immunology, Indiana University, School of Medicine, IN and Associate Member of Indiana University Cancer Center

1995: Award from Japanese society of In Born Error of Metabolism

1996: Grant support from Japanese Ministry of Education

1996: Travel award from the Japanese Ministry of Education

2003: Award from the Walther Cancer Institute for the postdoctoral competition (1<sup>st</sup> place)

1988-present: Japanese Society of Pediatrics (Board Certified Physician)

1993-present: Japanese Society of Human Genetics (Board Certified Physician)

2002-present: International Society of Experimental Hematology

2003-present: American Society of Hematology

2003-present: Society of Leukocyte Biology

**B. Selected peer-reviewed publications (in chronological order).** Do not include publications submitted or in preparation.

- S Fukuda**, S Tomatsu, K Sukegawa, T Sasaki, Y Yamada, T Kuwahara, H Okamoto, Y Ikedo, S Yamaguchi, T Orii. Molecular analysis of mucopolysaccharidosis type VII. J Inherit Metab Dis. 1991;14(5):800-4.
- S Tomatsu, **S Fukuda**, M Masue, K Sukegawa, T Fukao, A Yamagishi, T Hori, H Iwata, T Ogawa, Y Nakashima, Y Hanyu, et al. Morquio disease: isolation, characterization and expression of full-length cDNA for human N-acetylgalactosamine-6-sulfate sulfatase. Biochem Biophys Res Commun 1991 16;181(2):677-83.
- S Fukuda**, S Tomatsu, M Masue, K Sukegawa et al. Mucopolysaccharidosis type IVA. N-acetylgalactosamine-6-sulfate sulfatase exonic point mutations in classical Morquio and mild cases. J Clin Invest. 1992;90(3):1049-53.
- S Fukuda**, S Tomatsu, M Masuno, T Ogawa, A Yamagishi, GM Rezvi, K Sukegawa, N Shimozawa, Y Suzuki, N Kondo, K et al. Mucopolysaccharidosis IVA: submicroscopic deletion of 16q24.3 and a novel R386C mutation of N-acetylgalactosamine-6-sulfate sulfatase gene in a classical Morquio disease. Hum Mutat. 1996;7(2):123-34.
- S Fukuda**, S Tomatsu, A Cooper, JE Wraith, Z Kato, N Yamada et al. Mucopolysaccharidosis IVA (Morquio A): three novel small deletions in the N-acetylgalactosamine-6-sulfate sulfatase gene. Hum Mutat. 1996;8(2):187-90.
- S Fukuda**, N Shimozawa, Y Suzuki, Z Zhang, S Tomatsu, T Tsukamoto, N Hashiguchi, T Osumi, M Masuno, K Imaizumi, et al. Human peroxisome assembly factor-2 (PAF-2): a gene responsible for group C peroxisome biogenesis disorder in humans. Am J Hum Genet. 1996;59(6):1210-20.

7. **S Fukuda**, Y Yamada, M Nishimura, K Isogai, T Terada, M Iwata, N Shimozawa, et al. Marinesco-Sjogren syndrome associated with acute myeloblastic leukemia. Clin Genet. 1997 Apr;51(4):278-80.
8. **S Fukuda**, N Yamada, S Tomatsu, K Sukegawa, AM Montano, JJ Hopwood, et al. Mucopolysaccharidosis IVA: a novel splice acceptor site mutation in intron 4 of the N-acetylgalactosamine-6-sulfate sulfatase gene in an Afghanistan girl with classical Morquio disease. Jpn J Hum Genet. 1997;42(2):317-22.
9. **S Fukuda**, Y Yamada, K Isogai, T Terada, M Iwata, Y Takahashi, N Kondo. Chromosomal instability in Marinesco-Sjogren syndrome associated with acute myeloblastic leukemia. Clin Genet. 1998;53(2):153-4.
10. **S Fukuda**, Y Suzuki, N Shimozawa, Z Zhang, et al. Amino acid and nucleotide sequences of human peroxisomal enoyl-CoA hydratase: 3-hydroxyacyl-CoA dehydrogenase cDNA. J Inherit Metab Dis. 1998;21(1):23-8.
11. H Shibayama, N Anzai, SE Braun, **S Fukuda**, C Mantel, HE Broxmeyer. H-Ras is involved in the inside-out signaling pathway of interleukin-3-induced integrin activation. Blood. 1999;93(5):1540-8.
12. S Zhang, **S Fukuda**, Y Lee, G Hangoc, S Cooper, R Spolski, et al. Essential role of signal transducer and activator of transcription (Stat)5a but not Stat5b for Flt3-dependent signaling. J Exp Med. 2000;192(5):719-28.
13. **S Fukuda** and LM Pelus. Regulation of the inhibitor-of-apoptosis family member survivin in normal cord blood and bone marrow CD34(+) cells by hematopoietic growth factors: implication of survivin expression in normal hematopoiesis. Blood. 2001;98(7):2091-100.
14. **S Fukuda**, DW Wu, K Stark, LM Pelus. Cloning and characterization of a proliferation-associated cytokine-inducible protein, CIP29. Biochem Biophys Res Commun. 2002 Apr 5;292(3):593-600.
15. N Anzai, Y Lee, BS Youn, **S Fukuda**, et al. C-kit associated with the transmembrane 4 superfamily proteins constitutes a functionally distinct subunit in human hematopoietic progenitors. Blood. 2002;99(12):4413-21.
16. S Okabe, **S Fukuda**, HE Broxmeyer. Activation of Wiskott-Aldrich syndrome protein and its association with other proteins by stromal cell-derived factor-1alpha is associated with cell migration in a T-lymphocyte line. Exp Hematol. 2002;30(7):761-6.
17. **S Fukuda** and LM Pelus. Elevation of Survivin Levels by Hematopoietic Growth Factors Occurs in Quiescent CD34(+) Hematopoietic Stem and Progenitor Cells Before Cell Cycle Entry. Cell Cycle. 2002;1(5):322-6.
18. **S Fukuda**, RG Foster, SB Porter, LM Pelus. The antiapoptosis protein survivin is associated with cell cycle entry of normal cord blood CD34(+) cells and modulates cell cycle and proliferation of mouse hematopoietic progenitor cells. Blood. 2002;100(7):2463-71.
19. S Okabe, **S Fukuda**, HE Broxmeyer. Src kinase, but not the Src kinase family member p56lck, mediates stromal cell-derived factor 1 $\alpha$ /CXCL12-induced chemotaxis of a T cell line J Hemato.and Stem Cell Res 2002; 11:923-928
20. LM Pelus, H Bian, AG King, **S Fukuda**. Neutrophil-derived MMP-9 mediates synergistic mobilization of hematopoietic stem and progenitor cells by the combination of G-CSF and the chemokines GRO $\beta$ /CXCL2 and GRO $\beta$ <sub>7</sub>/CXCL2 $\Delta$ <sub>4</sub> Blood 2004.103:110-119
21. **S Fukuda**, CR Mantel, LM Pelus. Survivin regulates hematopoietic progenitor cell proliferation through p21<sup>WAF1/Cip1</sup> dependent and independent pathways. Blood 2004.103:120-127
22. A Merzouk, D Wong, H Salari, H Bian, **S Fukuda** and LM Pelus. Rational design of chemokine SDF-1 analogs with agonist activity for the CXCR4 receptor and the capacity to rapidly mobilize PMN and hematopoietic progenitor cells in mice. Letters in Drug Design and Discovery 2004, 1:126-134.
23. Z Wang, **S Fukuda** and LM Pelus. Survivin Regulates the p53 Tumor Suppressor Gene Family. Oncogene, 23: 8146-8153. 2004
24. **S Fukuda** and LM Pelus. Activated H-Ras Regulates Hematopoietic Cell Survival by Modulating Survivin. Biochem Biophys Res Commun. 2004. 323(2): 636-44.
25. S Okabe, **S Fukuda**, YJ Kim, M Niki, LM. Pelus, K Ohyashiki, PP. Pandolfi and HE. Broxmeyer. Stromal Cell-Derived Factor-1 $\alpha$ /CXCL12 Induced Chemotaxis of T Cells Involves Activation of the RasGAP-Associated Docking Protein p62Dok-1. Blood, 105(2): 474-480. 2005
26. **S Fukuda**, HE Broxmeyer and LM Pelus. Flt3 ligand and Flt3 Regulate Hematopoietic Cell Migration by Modulating the SDF-1 $\alpha$ (CXCL12)/CXCR4 Axis. Blood,105:3117-3126
27. LM Pelus, H Bian, **S Fukuda**, D Wong, A Merzouk, H Salari. The CXCR4 Agonist Peptide, CTCE-0021, Rapidly Mobilizes Polymorphonuclear Neutrophils and Hematopoietic Progenitor Cells into Peripheral Blood and Synergizes with G-CSF. Exp. Hematology, 33(3): 295-307. 2005
28. **S Fukuda** and LM Pelus. Growth Inhibitory Effect of Hcc-1/CIP29 is associated with Induction of Apoptosis, Not just with G<sub>2</sub>/M Arrest. Cellular and Molecular Life Sciences, 62(13):1526-7. 2005
29. Z Wang, J Sampath, **S Fukuda** and LM Pelus. Disruption of the Inhibitor of Apoptosis Protein, Survivin, Sensitizes Bcr-abl Positive Cells to STI571-induced Apoptosis. Cancer Research (In Press)

**BIOGRAPHICAL SKETCH**

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
William Scott Goebel, M.D., Ph.D.	Assistant Professor of Pediatrics

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EDUCATION ( <i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i> )			
INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Earlham College, Richmond, IN	B.A.	1987	Chemistry; Biology
Indiana University School of Medicine, Indianapolis, IN	M.D.	1995	Medicine
Indiana University School of Medicine, Indianapolis, IN	Ph.D.	1995	Microbiology and Immunology

**Certifications:**

1996 National Board of Medical Examiners  
 1998 American Board of Pediatrics  
 2004 American Board of Pediatrics, Sub-board of Pediatric Hematology/Oncology  
 Medical license, State of Indiana, #01048051 (1998 - present)

**Employment:**

1989 – 1993 **Research Assistant**, laboratory of Zacharie Brahmi, Ph.D., Indiana University School of Medicine, Indianapolis, IN. Dept. Head: D. C. Bauer. Non-tenured, full time position.  
 1995 – 1998 **Resident in Pediatrics**, St. Louis Children's Hospital, Washington University School of Medicine, St. Louis, MO. Dept. Head: Alan Schwartz. Non-tenured, full time position.  
 1998 – 2001 **Fellow in Pediatric Hematology/Oncology**, Indiana University School of Medicine, Indianapolis, IN. Dept. Head: Richard Schreiner. Non-tenured, full time position.  
 2001 – 2003 **Lecturer in Pediatrics**, Section of Pediatric Hematology/Oncology and Pediatric Stem Cell Transplantation Program, Indiana University School of Medicine, Indianapolis, IN. Dept. Head: Richard Schreiner. Non-tenured, full time position.  
 2003 – present **Assistant Professor of Pediatrics**, Section of Pediatric Hematology/Oncology and Pediatric Stem Cell Transplantation Program, Indiana University School of Medicine, Indianapolis, IN. Dept. Head: Richard Schreiner. Non-tenured, full time position.

**Honors:**

1987 All-College Honors, Earlham College  
 1987 Chemistry Departmental Honors, Earlham College  
 1987 Biology Departmental Honors, Earlham College  
 1987 Russell Malcolm Premedical Award, Earlham College  
 1987 J. Y. McCullough Scholarship, Indiana University School of Medicine  
 1988 - 1992 Research/Teaching Assistantship, Microbiology and Immunology, Indiana University  
 1992 M.D./Ph.D. Student Combined Degree Fellowship, Indiana University School of Medicine  
 1995 Indiana University School of Medicine Biomedical Paper Citation  
 2000 - 2002 William Kennedy Research Fellow of the National Childhood Cancer Foundation  
 2002 Trainee Travel Award, American Society for Clinical Investigation Annual Meeting

**Professional Societies:**

1995 - 2001 American Academy of Pediatrics  
 2000 - present American Society of Hematology  
 2001 - present Children's Oncology Group, Associate Member, Hematopoietic Stem Cell Transplant Committee  
 2002 - present International Society of Experimental Hematology  
 2002 - present American Society for Blood and Marrow Transplantation

**Publications:**

1. Bochan, M., **W.S. Goebel**, and Z. Brahmi. Stably transfected antisense granzyme B and perforin constructs inhibit human granule-mediated lytic ability. *Cell. Immunol.* 164:234-239, 1995.
2. Montel, A.H., M.R. Bochan, **W.S. Goebel**, and Z. Brahmi. Fas-mediated cytotoxicity remains intact in perforin and granzyme B antisense transfectants of a human NK-like cell line. *Cell. Immunol.* 165: 312-317, 1995.
3. **Goebel, W.S.**, R.H. Schloemer and Z. Brahmi. Target cell-induced perforin mRNA turnover in NK3.3 cells is mediated by multiple elements within the mRNA coding region. *Mol. Immunol.* 33: 341-349, 1996.
4. Hommel-Berrey, G.A., M.R. Bochan, A.H. Montel, **W.S. Goebel**, C.J. Froehlich and Z. Brahmi. Granzyme B

- independently of perforin mediates noncytolytic intracellular inactivation of vesicular stomatitis virus. *Cell. Immunol.* 180: 1-9, 1997.
5. Petersen, J.E., T.S.Hiran, **W.S. Goebel**, C. Johnson, R.C. Murphy, F.H. Azmi, A.F. Hood, J.B.Travers, and M.C.Dinauer. Enhanced Cutaneous Inflammatory Reactions to *Aspergillus fumigatus* in a Murine Model of Chronic Granulomatous Disease. *J. Invest. Dermatol.* 118:424-429, 2002.
  6. **Goebel, W.S.**, M.C. Yoder, N. Pech and M.C. Dinauer. Donor Chimerism and Stem Cell Function in a Murine Congenic Transplantation Model Following Low Dose Radiation Conditioning: Effects of a Retroviral-mediated Gene Transfer Protocol and Implications for Gene Therapy. *Exp. Hematol.* 30:1324-1332, 2002
  7. **Goebel, W.S.** and M.C. Dinauer. Retroviral-mediated Gene transfer and Nonmyeloablative Conditioning: Studies in a Murine X-linked Chronic Granulomatous Disease Model. *J. Ped. Hematol. Oncol.* 24:787-790, 2002.
  8. **Goebel, W.S.**, N. Pech, and M.C. Dinauer. 2004. Stable Long-term Gene Correction with Low-dose Radiation Conditioning in Murine X-linked Chronic Granulomatous Disease. *Blood Cells Mol. Dis.*; 33:365-71, 2004.
  9. **Goebel, W.S.**, N. Pech, J.L. Meyers, E.F. Srour, M.C. Yoder and M.C. Dinauer. 2004. A Murine Model of Antimetabolite-based, Submyeloablative Conditioning for Bone Marrow Transplantation: Biologic Insights and Potential Applications. *Exp. Hematol.*; 32:1255-64, 2004.
  10. **Goebel, W.S.**, L.A. Mark, S.D. Billings, J.L. Meyers, N. Pech, J.B. Travers, and M.C. Dinauer. Gene Correction Reduces Cutaneous Inflammation and Granuloma Formation in Murine X-Linked Chronic Granulomatous Disease. *J. Invest. Dermatol.*; 125:705-10, 2005.
  11. **Goebel, W.S.**, J.H. Conway, P. Faught, S.T. Vakili, and P.R. Haut. Disseminated toxoplasmosis resulting in graft failure in a seronegative cord blood stem cell transplant recipient – case report and discussion of toxoplasmosis in stem cell transplant recipients. *Pediatr Blood Cancer*; in press.

#### **Review Articles :**

1. **Goebel, W.S.**, A. Kume and M.C. Dinauer. Gene Therapy for Chronic Granulomatous Disease and Leukocyte Adhesion Deficiency. *Int. J. Pediatric Hematol. Oncol.* 7: 359-372, 2001
2. **Goebel, W.S.** and M.C. Dinauer. Gene therapy for Chronic Granulomatous Disease. *Acta Haematologica* 110: 86-92, 2003.
3. Barese, C.N., **W.S. Goebel** and M.C. Dinauer. Gene therapy for chronic granulomatous disease. *Expert Opin Biol Ther.* 4(9):1423-34, 2004.

#### **Selected abstracts/presentations:**

1. **Goebel, W.S.**, G. Hommel-Berrey, and Z. Brahmi. 1992. Lymphokine-activated killer cells do not induce degradation of viral or cellular RNA in targets in which DNA fragmentation occurs. Annual American Association of Immunologists Conference, April 1992 (poster presentation).
2. **Goebel, W.S.** and Z. Brahmi. 1993. Partial inhibition of perforin expression in two NK-like cell lines by stable antisense transfection does not lead to a concomitant decrease in cytolytic activity. Annual Meeting, American Association of Immunologists (AAI)/ Clinical Immunology Society (CIS), May 1993.
3. **Goebel, W.S.**, N. Pech and M.C. Dinauer. 2000. Effects of low dose irradiation and retroviral-mediated gene transfer (RMGT) on donor chimerism and gene correction in a murine X-linked chronic granulomatous disease (X-CGD) model. *Exp. Hematol.* 28:1499-500. Annual Meeting, International Society of Experimental Hematology, July 2000 (oral presentation).
4. **Goebel, W.S.**, N. Pech, E.F. Srour and M.C. Dinauer. 2000. Use of paired dose 5-fluorouracil as a conditioning regimen for marrow transplantation in a syngeneic mouse model. *Blood* 96 (11):171a Annual Meeting, American Society for Hematology, December 2000 (poster presentation).
5. **Goebel, W.S.**, J.B. Travers, N. Pech and M.C. Dinauer. 2001. Retroviral-mediated gene transfer (RMGT) reduces cutaneous inflammation and granuloma formation in a murine model of X-linked chronic granulomatous disease (X-CGD) *Blood* 98 (11): 695a. Annual Meeting, American Society for Hematology, December 2001 (poster presentation).
6. **Goebel, W.S.**, R.P. Nelson, D.J. Gowan, P.J. Towell, K.A. Robertson and P.R. Haut. Serial transplantation resulting in tolerance to an unrelated cord blood graft. Annual Meeting, American Society for Hematology, December 2003 (poster presentation).
7. **Goebel, W.S.**, N. Pech, J.L. Meyers and M.C. Dinauer. Use of an antimetabolite-based, submyeloablative conditioning regimen for transplantation of murine marrow cells for gene therapy. Annual Meeting, American Society for Hematology, December 2003.
8. Meyers, S.E., J.L. Meyers and **W.S. Goebel**. Homing efficiency in two models of submyeloablative conditioning and correlation with long-term engraftment. Annual Meeting, American Society for Hematology, December 2004 (poster presentation).
9. Barese, C.S., **W.S. Goebel**, N.K. Pech, J.L. Meyers and M.C. Dinauer. Granulocyte colony-stimulating factor prior

to low-dose total body irradiation as conditioning regimen in hematopoietic cell transplantation for gene therapy. Annual Meeting, American Society for Hematology, December 2004 (poster presentation).

## **Research Projects Ongoing or Completed During the Last 3 Years:**

### **ONGOING RESEARCH ACTIVITIES**

1. Source of Support: National Institutes of Health (NHLBI)
  2. Identification #: 1 K08 HL075253
  3. Project Title: Factors Influencing Engraftment in Submyeloablated Hosts
  4. Principal Investigator: W. Scott Goebel
  5. Project Period: 8/2/05-7/31/10  
Description of Project: The objective of this application is to determine mechanisms governing the engraftment of transduced HSC in two models of submyeloablative conditioning for murine hosts.
- 
1. Source of Support: Clarian Health Partners, Inc.
  2. Identification #: VFR-145
  3. Project Title: Mechanisms of engraftment of transduced HSC
  4. Principal Investigator: W. Scott Goebel
  5. Project Period: 2/1/03-1/31/06  
Description of Project: The specific aim of this proposal is to identify requirements for effective engraftment of retrovirus transduced HSC into submyeloablated hosts using a murine model by examining adhesion molecule expression, cell cycle phenotype, and homing of fresh marrow and transduced murine marrow.
- 
1. Source of Support: Centers of Excellence in Molecular Hematology
  2. Project Title: The role of periostin in murine hematopoiesis
  3. Principal Investigator: W. Scott Goebel
  4. Project Period: 12/1/04-11/30/05
  5. Description of Project: The specific aim of this proposal is to study the extent to which hematopoiesis is modified by disruption of the periostin gene, which has been demonstrated to regulate osteoblast adhesion and differentiation.

### **COMPLETED RESEARCH SUPPORT**

1. Source of Support: National Childhood Cancer Foundation
  2. Identification #: William Kennedy Research Fellowship
  3. Project Title: Nonmyeloablative conditioning regimens for gene therapy
  4. Principal Investigator: W. Scott Goebel
  5. Project Period: 7/1/00-6/30/02  
Description of Project: The goal of the research fellowship was to develop alternatives to myeloablative conditioning for use in transplantation of transduced marrow cells for gene therapy.
- 
1. Source of Support: American Cancer Society (institutional)
  2. Identification #: IRG-84-002-19
  3. Project Title: Development of a murine marrow transplantation assay
  4. Principal Investigator: W. Scott Goebel
  5. Project Period: 9/1/02-8/31/04  
Description of Project: The specific aim of this project is to develop a competitive repopulation assay using nonmyeloablated hosts, to directly measure fresh donor stem cell function and to determine the effects of a widely used method of retroviral-mediated gene transfer on engraftment in submyeloablated hosts.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Eri Hashino		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME EHASHINO			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Tokyo Woman's Christian University	B.A.	1981	Experimental Psychology
Osaka University	M.S.	1985	Neuroethology
Nagoya University	Ph.D.	1991	Neurobiology
State University of New York at Buffalo	Post-Doc	1991-1993	

**A. POSITIONS AND HONORS****Positions and Employment**

- 1981-1983 Research Assistant, Department of Neuroscience, Osaka University  
 1994-2002 Research Scientist, Center for Hearing and Deafness and Assistant Professor  
 Department of Communicative Disorders & Sciences, SUNY at Buffalo  
 2002-present Associate Professor and Ruth C. Holton Scholar, Department of Otolaryngology-HNS  
 Indiana University School of Medicine  
 2002-present Associate Professor, Department of Anatomy and Cell Biology (secondary appointment)  
 Indiana University School of Medicine  
 2003-present Primary Investigator, Stark Neurosciences Research Institute  
 Indiana University School of Medicine

**Awards and Other Professional Activities**

- 2002 NASA Developmental Biology Review Panel  
 2002-present Ruth C. Holton Scholar of Otolaryngology, Indiana University School of Medicine  
 2003, 2005 NIDCD/NIH Special Emphasis Panel  
 2003-2004 NSF Developmental Neuroscience Advisory Panel  
 2005 James A. Shannon Director's Award, NIDCD/NIH  
 2005 NIH CSR/AUD Study Section

**B. SELECTED PUBLICATIONS** (from a total of 32 peer-reviewed papers and book chapters)

- Hashino E**, Tanaka Y, Salvi RJ, Sokabe M (1992) Hair cell regeneration in the adult budgerigar after kanamycin ototoxicity. *Hear. Res.* 59: 46-58.  
**Hashino E**, Sokabe M, Tanaka Y (1992) Function-structure correlation during recovery from aminoglycoside ototoxicity in avian auditory system. In: A. Dancer, D. Henderson, R. Salvi, and R. P. Hamernik (Eds.), *Noise-Induced Hearing Loss*, Mosby Year Book, St. Louis, pp. 228-236.  
**Hashino E**, Salvi RJ (1993) Changing spatial patterns of DNA replication in the noise-damaged chick cochlea. *J. Cell Sci.* 105: 23-31.  
 Chen L, Salvi RJ, **Hashino E** (1993) Recovery of CAP threshold and amplitude in adult chickens following kanamycin ototoxicity. *Hear. Res.* 69: 15-24.  
 Salvi RJ, Saunders SS, **Hashino E**, Chen L (1994) Discharge patterns of cochlear ganglion neurons following kanamycin-induced hair cell loss and regeneration: Tuning and spontaneous activity. *J. Comp. Physiol. A* 174: 351-369.  
**Hashino E**, Shero M (1995) Endocytosis of aminoglycoside antibiotics in sensory hair cells. *Brain Res.*

704: 135-140.

- Hashino E**, TinHan EK, Salvi RJ (1995) Base-to-apex gradient of cell proliferation in the chick cochlea following kanamycin induced hair cell loss. *Hear. Res.* 88: 156-168.
- Salvi RJ, Chen L, **Hashino E**, Saunders SS (1995) Regeneration of sensory and supporting cells: Relationship to physiological and psychological measures. In: G.A. Manley, G.M. Klump, C. Koppl, H. Fastl and H. Oeckinghaus (Eds.), *Advances in Hearing Research*, World Scientific, pp.73-84.
- Hashino E** (1996) Resistance of regenerated hair cells to aminoglycoside toxicity. In: R.J. Salvi, D. Henderson, F. Fiorino and V. Colletti (Eds.), *Auditory System Plasticity and Regeneration*, Thieme Medical Publishers, New York, pp. 190-201.
- Hashino E**, Salvi RJ (1996) Regenerated hair cells exhibit a transient resistance to aminoglycoside toxicity. *Brain Res.* 720: 172-182.
- Trautwein PG, Salvi RJ, Miller K, Shero M, **Hashino E** (1996) Partial recovery of distortion product otoacoustic emissions in adult chickens following acoustic overstimulation. *Audiology & Neuro-Otology* 1: 86-103.
- Hashino E**, Shero M, Salvi RJ (1997) Lysosomal targeting and accumulation of aminoglycoside antibiotics in sensory hair cells. *Brain Res.* 777: 75-85.
- Trautwein PG, **Hashino E**, Salvi RJ (1998) Regenerated hair cells become functional during continuous administration of kanamycin. *Audiology & Neuro-Otology* 3: 229-239.
- Shero M, Salvi RJ, Chen L, **Hashino E** (1998) Excitotoxic effect of kainic acid on chicken cochlear afferent neurons. *Neurosci. Letters* 257: 81-84.
- Hashino E**, Dolnick RY, Cohan CS (1999) Developing vestibular ganglion neurons switch trophic sensitivity from BDNF to GDNF after target innervation. *J. Neurobiol.* 38: 414-427.
- Hashino E**, Johnson EM Jr, Milbrandt J, Shero M, Salvi RJ, Cohan CS (1999) Multiple actions of neurturin correlate with spatiotemporal patterns of Ret expression in developing chick cranial ganglion neurons. *J. Neurosci.* 19: 8476-8486.
- Sun H, Salvi RJ, Ding DL, **Hashino E**, Shero M, Zheng XY (2000) Excitotoxic effect of kainic acid on otoacoustic emissions and cochlear potentials of chickens. *J. Acoust. Soc. Am.* 107: 2136-2142.
- Hashino E**, Shero M, Salvi RJ (2000) Lysosomal augmentation during aminoglycoside uptake in cochlear hair cells. *Brain Res.* 887: 90-97.
- Sun H, **Hashino E**, Ding DL, Salvi RJ (2001) Reversible and irreversible damage to cochlear afferent neurons by kainic acid excitotoxicity. *J. Comp. Neurol.* 430: 172-181.
- Hashino E**, Shero M, Junghans D, Rohrer H, Milbrandt J, Johnson EM Jr (2001) GDNF and neurturin are target-derived factors essential for cranial parasympathetic neuron development. *Development* 128: 3773-3782.
- Romand R, **Hashino E**, Dolle P, Chambon P, Ghyselinck NB (2002) The retinoic acid receptors RAR $\alpha$  and RAR $\gamma$  are required for inner ear development. *Mech. Dev.* 119: 213-223.
- Romand R, Niederreither K, Abu-Abed S, Petkovich M, Fraulob V, **Hashino E**, Dolle P (2004) Complementary expression patterns of retinoic acid synthesizing and -metabolizing enzymes in prenatal mouse inner ear structures. *Gene Expr. Patterns* 4: 123-133.
- Kondo T, Johnson SA, Yoder MC, Romand R, **Hashino E** (2005) Sonic hedgehog and retinoic acid synergistically promote sensory fate specification from bone marrow-derived pluripotent stem cells. *Proc. Natl. Acad. Sci. USA* 102: 4789-4794 (**Cover article, also featured in "This Week in PNAS"**).
- Romand R, Dolle P, **Hashino E** (2005) Retinoid signaling in inner ear development. *J. Neurobiol.* (in press).
- Romand R, Kondo T, Fraulob V, Petkovich M, Dolle P, **Hashino E** (2005) Dynamic expression of retinoic acid synthesizing and metabolizing enzymes in the developing mouse inner ear. *J. Comp. Neurol.* (accepted pending minor revision).
- Matsuoka AJ, Kondo T, Miyamoto RT, **Hashino E** (2005) Transplantation of bone marrow-derived stem cells in the Mongolian gerbil cochlea. *Laryngoscope* (accepted).
- Qiu M, Aloor HL, Hu X, Chestovich PJ, Kondo T, **Hashino E** (2005) Expression of Nkx6.1 and Olig transcription factors in the developing inner ear. *Gene Expr. Patterns* (in revision).
- Clarke JM, Aloor HL, Chan RJ, **Hashino E** (2005) Temporal gene and protein expression profile in murine embryonic stem cells during neural differentiation. (in preparation).

## C. RESEARCH SUPPORT

### Ongoing Research Support

IBN 0324243 Hashino, Eri (PI) 11/1/02-4/30/06  
NSF

“GDNF Family Ligands in Parasympathetic Neuron Development”

The goal of this project is to delineate novel functions of GDNF in the formation and differentiation of cranial parasympathetic neurons.

R55 DC 007390 Hashino, Eri (PI) 3/1/05-2/28/07  
NIH/NIDCD

“Adult Stem Cells in the Inner Ear”

The goal of this project is to investigate the interactions between marrow-derived pluripotent stem cells and the inner ear microenvironment.

Biomedical Research Grant Hashino, Eri (PI) 3/1/05-2/28/06

Indiana University School of Medicine

“Integration of Adult Stem Cells in the Inner Ear”

The goal of this intramural grant is to obtain additional preliminary data that will strengthen the PI's pending R01 application.

### Completed Research Support

R01 DC 003900 Hashino, Eri (PI) 8/1/99-7/31/05  
NIH/NIDCD

“Cellular Mechanisms of Ototoxicity”

The goals of this project are to elucidate the uptake pathway of aminoglycoside antibiotics in cochlear hair cells and to test the possibility that selective inhibition of aminoglycoside uptake results in prolonged survival of hair cells.

R21 DC 005507 Hashino, Eri (PI) 5/1/02-4/30/05  
NIH/NIDCD

“Neural Stem Cells in the Otocyst”

The goal of this project is to characterize neural stem cells that are isolated from the developing inner ear.

### Pending Research Support

R01 DC 007390 Hashino, Eri (PI) 12/1/05-11/30/10 (Score within automatic payline received)  
NIH/NIDCD

“Adult Stem Cells in the Inner Ear”

The goal of this project is to investigate the interactions between marrow-derived pluripotent stem cells and the inner ear microenvironment.

**BIOGRAPHICAL SKETCH**

NAME	POSITION TITLE
Dongming Hou, MD, PhD	Assistant Scientist, Indiana University

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
HeBei Medical University, Shijiazhuang, China	MD	1980-1985	Medicine
Academic Teaching Hospital, HeBei Medical University	Resident	1985-1990	Internal Medicine
Hebei Medical University	MS	1990-1993	Cardiovascular Disease Research
Beijing Medical University	PhD	1993-1996	Cardiology & Vascular Biology
University of Heidelberg, Germany	Post-doc Fellowship	1996-1998	Interventional and Basic Cardiovascular Research
Indiana university School of Medicine	Post-doc Fellowship	1998-2001	Interventional Cardiology Research

**Positions**

1990-1993 Cardiology Faculty, Academic teaching Hospital of HeBei Medical University, Shijiazhuang, China  
 2001-Present Assistant Scientist, Department of Medicine, Indiana University School of Medicine

**Honors**

1998-2001 Cryptic Masons Medical Research Foundation fellowship

**Selected Publications**

- Liu Kunshen, **Hou Dongming**, Li Xiaotao, Jin Fuchang. Rapid bedside temporary pacing by the right supraclavicular subclavian vein approach. Am J Cardiol 1993; 71(15): 1234-1235
- Ralf Kinscherf, Hans-Peter Deigner, Claus Usinger, Johannes Pill, Martin Wagner, Huse Kamencic, **Dongming Hou**, Min Chen, Walther Schmiedt, Michael Schrader, Gyula Kovacs, Kanefusa Kato, Jürgen Metz. Induction of mitochondrial manganese superoxide dismutase in macrophages by oxidized LDL: is relevance in atherosclerosis of humans and heritable hyperlipidemic rabbits. The FASEB Journal 1997; 11(14): 1317-1328
- Ralf Kinscherf, Ralf Claus, Martin Wagner, Christof Gehrke, Huse Kamencic, **Dongming Hou**, Olaf Nauen, Walther Schmiedt, Gyula Kovacs, Johannes Pill, Jürgen Metz and Hans-Peter Deigner. Apoptosis caused by oxidized LDL is manganese superoxide dismutase and p53 dependent. The FASEB Journal 1998; 6(12): 461-467
- Ralf Kinscherf, Martin Wagner, Huse Kamencic, **Dongming Hou**, Rainer A. Schiele, Hans-Peter Deigner, Jürgen Metz. Characterization of apoptotic macrophages in atheromatous tissue of humans and heritable hyperlipidemic rabbits. Atherosclerosis 1999; 144: 33-39.
- Dongming Hou**, Pamela I. Rogers, Philip M. Toleikis, William Hunter, Keith L. March. Intrapericardial space delivery of paclitaxel inhibits neointimal proliferation and promotes arterial enlargement after porcine coronary overstretch. Circulation 2000; 102: 1575-1581.
- Hans-Peter Stoll, Gary D. Hutchins, Wendy L. Winkle, Anne T. Nguyen, **Dongming Hou**, C. Robert Appledorn, Bernd Romeike, Keith L. March. Liquid-Filled Balloon Brachytherapy Using 68Ga Is Effective and Safe Because of the Short 68-Minute Half-Life. Results of a Feasibility Study in the Porcine Coronary Overstretch Model. Circulation. 2001;103:1793-1798.

7. Riley JN, Dickson TJ, **Hou Dongming**, Rogers P, March KL, McNally-Heintzelman KM. Improved laser-assisted vascular tissue fusion using light-activated surgical adhesive in a porcine model. Biomed Sci Instrum 2001; 37:451-456.
8. SangHong Beak, Joseph A. Hrabie, Larry K. Keefer, Khawar Mehdi, **Dongming Hou**, Naomi Fingberg, Rodney Rhoades, Keith L. March. Augmentation of intrapericardial nitric oxide level by a prolonged release NO donor reduces luminal narrowing after porcine coronary angioplasty. Circulation 2002; 105: 2778-2784.
9. **Dongming Hou**, Fiona McLaughlin, Mary thiesse, Pamela Rogers, Rosa Johnson, Jijun Wang, Eric Rothe, Michael E. Coleman, Keith L. March. Widespread myocardial transfection by plasmid encoding del-1 following retrograde coronary venous delivery. Catheter Cardio Inte 2003;58: 207-211.
10. **Dongming Hou**, Keith L. March. A novel percutaneous technique for accessing the normal pericardium: a single center successful experience of 53 porcine procedure. (J Invasive Cardio 2003;15: 13-16.)
11. Strecker EP, Song HY, Kang SG, **Dongming Hou**, Schumacher M. First experimental results with a new type of stent: the double-coil device. Cardiovasc Intervent Radiol 2003 Jun 3;26(3): 269-272.
12. **Dongming Hou**, Alexander E. Marsh, Keith L. March. Intrapericardial ethanol delivery inhibits neointimal proliferation after porcine coronary overstretch. Chinese Medical Journal (Taipei) 2003;66:637-642.
13. Ping Zhang, Keith L. March, **Dongming Hou**. Physical Training and Cardioprotection. Chinese Journal of Sports Medicine 2003; 22: 378-382.
14. **Dongming Hou**, Hugh Narciso, Kirti Kamdar, Ping Zhang, Bruce Barclay, Keith L. March. Reducing neointimal proliferation by a stent-based delivery of nitric oxide in a porcine carotid overstretch injury model. Cardiovasc Intervent Radiol 2005;28:60-65.
15. Eyas Al-Shaykh Youssef, Ping Zhang, Pamela Rogers, Patrice Tremble, Joe Rokovich, Brian Johnstone, Keith L. March, **Dongming Hou**. Enhancing Myocardial Plasmid Expression by Retrograde Coronary Venous Delivery. Catheter Cardio Inte 2005; 65:528-534.
16. **Dongming Hou**, Eyas Al-Shaykh Youssef, Todd J. Brinton, Ping Zhang, Pamela Rogers, Erik Price, Alan C. Yeung, Brian H. Johnstone, Paul G. Yock, Keith L. March. Radiolabelled Cell Distribution following Intramyocardial, Intracoronary, and Interstitial Retrograde Coronary Venous Delivery: Implications for Current Clinical Trials. Circulation 2005;112 (suppl): I-150-I-156.

#### **Book Chapters:**

1. **Hou DM, March KL**. The Intrapericardial Approach for Therapeutic Angiogenesis. In: Kornowski, L, ed. Handbook of Myocardial Revascularization. London: Martin Dunitz Publishers. 1999; 189-200.
2. **Hou DM, March KL**. Intrapericardial Drug Delivery for Prevention of Restenosis. Camenzind E and De Scheerder I, eds. Handbook of Local Drug Delivery for Coronary Diseases. London: Taylor & Francis, 2005; 549-558.

#### **Ongoing Research Support**

- Medtronic, Inc., *Pilot Study for Therapeutic Myocardial Angiogenesis*, 2004-2006, P.I.
- Vascular Architects, Inc., *Pilot Study of Generation II Med-aSpire in Swine Carotid Injury Model, 2004-2005*, P.I.
- R24 RR 13223-07 (Michael Sturek, P.I.), 2004-2008, 10% Co-I.

#### **Completed Research Support**

- Vascular Architects, Inc., *Pilot Study of Nitric Oxide (NO) Eluted by an ePTFE-Covered Stent in Swine Carotids*, 2002-2003, P.I. This grant evaluates the toxicity and efficacy of a drug-coated stent. There is no overlap with the aims of the present application.
- Vascular Architects, Inc., *Pilot Study of Nitric Oxide (NO) Eluted by an ePTFE-Covered Stent in Swine iliac artery*, 2003-2004, P.I. This grant evaluates the toxicity and efficacy of a drug-coated stent. There is no overlap with the aims of the present application.

**BIOGRAPHICAL SKETCH**

NAME <b>David Aaron Ingram, Jr., M.D.</b>	POSITION TITLE <b>Assistant Professor of Pediatrics</b>
eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Brown University, Providence, Rhode Island	B.A.	5/1989	Religious studies
Vanderbilt Univ. School of Med., Nashville, TN	Master of Theological M.D.	1992 5/1994	Theology/Ethics Medicine
Vanderbilt Univ. School of Med., Nashville, TN	Resident	1994-1997	Pediatrics
Univ. of CA at San Francisco, CA	Chief	1997-1998	Pediatrics
Univ. of CA at San Francisco, CA	Fellow	1998-2002	Neonatology

**A. Positions and Honors.**

- 1989 Magna Cum Laude – Brown University
- 1989 Justin Potter Medical Scholarship, Vanderbilt Univ. School of Med., Nashville, TN, Merit based
- 1990 Dan May Research Scholar in Cardiology, Vanderbilt Univ. School of Med., Nashville, TN
- 1991 Deans Scholarship, Vanderbilt Divinity School, Nashville, TN, Merit based
- 1995 Trainee Investigator Award for Excellence in Scientific Research, Clinical Research Meeting, San Diego, CA
- 1995 Julius R. Krevans Prize for Clinical Excellence in Residency, Univ. of CA at SF, San Francisco, CA
- 1998-2001 Pediatric Scientist Development Program Award
- 2000 Travel Award from the American Society of Hematology
- 2001 Member, Alpha Omega Alpha Honor Medical Society
- 2002 Young Investigator Travel Award, American Society of Clinical Investigation
- 2002 Travel Award, National Neurofibromatosis Foundation
- 2002 NIH Young Investigator Award, Perinatal Research Society
- 2002 Clinical Investigator Award, National Cancer Institute
- 2002 Member, Program of Comparative Medicine
- 2003 Basil O'Connor Award, March of Dimes
- 2004 Department of Defense Study Section – NF1 and NF2, Department of Defense
- 2005 Department of Defense Study Section – NF1 and NF2, Department of Defense
- 2005 Young Investigator Scholarship Award, American Society for Clinical Investigation
- 2005 Executive Committee Member, Indiana University Cancer Center
- 2005 Executive Committee Member, Indiana Center for Vascular Biology and Medicine

**B. Selected peer-reviewed publications (in chronological order).**

- Forman MB, Pitarys CJ, Vilibill HD, Lambert T, **Ingram DA**, Murray JJ. Pharmacological perturbation of neutrophils by Fluosol-DA results in a sustained reduction in infarct size in the canine model of reperfusion injury. *Journal of the American College of Cardiology* 19:205-215, 1992.
- Ingram DA**, Forman MB, Murray JJ. Phagocytic activation of human neutrophils by the detergent component of Fluosol. *American Journal of Pathology* 5:1082-1087, 1992.
- Forman MB, **Ingram DA**, Murray JJ. Attenuation of myocardial reperfusion injury by perfluorochemical emulsions. *Clinical Hemorheology* 12:121-140, 1992.
- Forman MB, **Ingram DA**, Murray J. Role of perfluorochemical emulsions in the treatment of myocardial reperfusion injury. *American Heart Journal* 124:1347-1357, 1992.
- Ingram DA**, Forman MB, Murray J. Activation of complement by Fluosol attributable to the pluronic detergent micelle structure. *Journal of Cardiovascular Pharmacology* 22:456-461, 1993.

6. Goetzl EJ, Xia M, **Ingram DA**, Kishiyama L, Kaltrieder HB, Byrd PK, Ichikawa S, Sreedharan SP. Neuropeptide signaling of lymphocytes in immunological responses. *International Archives of Allergy and Immunology* 107:202-204, 1995.
7. Kaltreider HB, Ichikawa S, Byrd PK, **Ingram DA**, Kishiyama JL, Sreedharan SP, Warnock ML, Beck JM, Goetzl EF. Upregulation of neuropeptides and neuropeptide receptors in a murine model of immune inflammation in lung parenchyma. *American Journal of Respiratory and Cellular and Molecular Biology* 16:133-144, 1997.
8. **Ingram DA**, Yang F, Travers JB, Wenning MJ, Hiatt K, New S, Hood A, Shannon K, Williams DA, Clapp DW. Haploinsufficiency at *Nf1* modulates c-kit signaling in melanocytes and mast cells *in vivo*. *Journal of Experimental Medicine*. 191(1):181-187, 2000.
9. Hiatt, K, **Ingram DA**, Zhang YY, Bollag G, Clapp DW. Neurofibromin GAP related domains (GRDs) restore normal growth in *Nf1*  $-/-$  cells. *Journal of Biological Chemistry* 276(10):7240-7245, 2001.
10. **Ingram DA**, Hiatt KK, King A, Fisher L, Shivakumar R, Derstine C, Wenning MJ, Diaz B, Travers JB, Hood A, Marshall M, Williams DA, Clapp DW. Hyperactivation of p21ras and the hematopoietic specific Rho GTPase, Rac2, cooperate to alter the proliferation of neurofibromin deficient mast cells *in vivo*. *Journal of Experimental Medicine*. 194(1):57-70, 2001.
11. **Ingram DA**, Zhang L, McCarthy J, Wenning MJ, Fisher L, Clapp DW, Kapur, R. Neurofibromin (NF1) tumor suppressor gene functions as a GAP for Ras in T cells: Functional and biochemical consequences of *Nf1* heterozygosity and homozygosity. *Blood* 100(10):3656-3667, 2002.
12. **Ingram DA\***, Wenning MJ, Shannon K, Clapp DW. Leukemic potential of doubly mutant *Nf1* and *Wv* hematopoietic cells. *Blood* 101(5):1984-1986, 2003. \*Corresponding author
13. Tan BL, Yazicioglu MN, **Ingram DA**, McCarthy J, Borneo J, Williams DA, Kapur R. Genetic evidence for convergence of c-kit- and  $\alpha 4$  integrin-mediated signals on class IA PI-3kinase and the Rac pathway in regulating integrin-directed migration in mast cells. *Blood* 101(12):4725-4732, 2003.
14. Huddleston H, Tan BL, Yang FC, White H, Wenning MJ, Orazi A, Yoder MC, Kapur R, **Ingram DA**. Functional p85 $\alpha$  gene is required for normal murine fetal erythropoiesis. *Blood* 102(1):142-5, 2003.
15. Yang FC, **Ingram DA\*\***, Chen S, Hingtgen CM, Ratner N, Monk KR, Clegg T, White H, Mead L, Wenning MJ, Williams DA, Kapur R, Atkinson SJ, Clapp DW. Neurofibromin-deficient Schwann cells secrete a potent migratory stimulus for *Nf1*  $+/-$  mast cells. *Journal of Clinical Investigation*. 112: 1851-1861, 2003. \*\*Co-first and corresponding author.
16. Hiatt KK, **Ingram DA\*\***, Huddleston H, Kapur R, Spaudau D, Clapp DW. Loss of *Nf1* reduces Fas ligand-mediated apoptosis in murine bone marrow derived mast cells in response to stem cell factor. *American Journal of Pathology*. 164(4): 1471-9, 2004. \*\*Co-first author.
17. Li F, Li W, Johnson SA, **Ingram DA**, Yoder MC, Badylak SF. Low molecular weight peptides derived from extracellular matrix as chemoattractants for primary endothelial cells. *Endothelium*. 11(3-4): 199-206, 2004.
18. **Ingram DA\***, Mead L, Tanaka H, Meade V, Mortell K, Fenoglio A, Pollok K, Ferkowicz MJ, Gilley D, Yoder MC. Identification of a Novel Hierarchy of Human Endothelial Progenitor Cells Utilizing a Umbilical and Adult Peripheral Blood. *Blood*, Nov 2004; 104: 2752-2760. \*Corresponding author
19. **Ingram DA\*\***, Mead LE, Moore DB, Woodard W, Fenoglio A, Yoder MC. Vessel wall derived endothelial cells rapidly proliferate because they contain a complete hierarchy of endothelial progenitor cells. *Blood*, 2005 Apr 1;105(7):2783-6. \*Corresponding author
20. Khalaf W, White H, Wenning MJ, Orazi, A, Kapur R, **Ingram DA**. K-Ras is essential for Fetal Erythropoiesis *In Vivo*. *Blood*, 2005 May 1;105(9):3538-41
21. Munugalavadla V, Borneo J, **Ingram DA**, Kapur R. p85 $\alpha$  subunit of Class IA PI-3 Kinase is crucial for macrophage growth and migration. *Blood*, 2005 Jul 1;106(1):103-9. Epub 2005 Mar 15.
22. Yu X, Chen S, Potter OL, Murthy SM, Li J, Pulcini JM, Ohashi N, Winata T, Everett ET, **Ingram D**, Clapp WD, Hock JM. Neurofibromin and its inactivation of Ras are prerequisites for osteoblast functioning. *Bone*. 2005 May;36(5):793-802. Epub 2005 Mar 29
23. Haneline LS, White H, Yang FC, Orschell C, Kapur R, **Ingram DA**. Genetic Reduction of Class IA PI-3 Kinase Activity Alters Fetal Hematopoiesis and Competitive Repopulating Ability of Hematopoietic Stem Cells *In Vivo*. *Blood*, conditionally accepted.
24. **Ingram DA**, Caplice NM, Yoder MC. Unresolved questions, changing definitions, and novel paradigms for defining endothelial progenitor cells. *Blood*. 2005 May 19; [Epub ahead of print]

**C. Research Support - Ongoing or Completed During the Last 3 Years****Prior Grant Support:**

- Biochemical and Phenotypic Effects of Heterozygous Inactivation of *Nf1* in Mast Cells. U.S. Army, Neurofibromatosis Research Program. DAMD17-01-1-0711, 9/17/01-10/16/04, Annual Direct Costs \$144,386. DW Clapp, Principal investigator, DA Ingram, nested investigator. Effort: 50%
- Ras-P13K Pathway in *Nf1* Hematopoiesis and Leukemogenesis, March of Dimes, Basil O'Connor Award, 5FY2003162, 2/1/2003-1/31/2005, Annual Direct Costs \$75,000. DA Ingram, principal investigator. 10% effort
- "Nf1 +/- Mast Cells Promote Inflammation and Angiogenesis", National Cancer Institute (NCI), NIH grant RO1 CA74177-supplemental project for RO1, 8/1/03—7/31/05, Annual Direct Cost \$120,000, D. W. Clapp, Program leader: D. Ingram, Principal Investigator/Project 3, Effort 2%

**Current Grant Support:**

- "Ras-PI3K Pathway in NF1 +/- Hematopoiesis and Leukemia", National Institutes of Health (NIH), 1 K08 CA096579-01, 7/1/02—6/30/07, Annual Direct Cost \$122,028, D. Ingram, Principal Investigator, Effort 75%
- "Function of Neurofibromin in Endothelial Cells", Department of Defense, NF043019, 1/1/05-1/1/08, Annual Direct Cost \$150,000, D. Ingram, Principal Investigator, Effort 10%
- "Role of NF1 in Angiogenesis and Vascular Smooth Muscle", NIH Program Project Grant – Project 3, 10/1/05-9/30/10, Annual Direct Cost \$250,000, D. Ingram, Principal Investigator/Project 3, Effort 30%
- "Cord Blood Stem Cell Expansion Ex Vivo With Endothelial Progenitor Cells", Showalter Trust Grant-Indiana University School of Medicine, 7/1/05-7/1/06, Annual Direct Cost \$60,000, D. Ingram, Principal Investigator, Effort 2%
- "Cord Blood Stem Cell Expansion Ex Vivo With Endothelial Progenitor Cells", STTR Grant, NIH, 7/1/05-7/1/06, Annual Direct cost \$100,000, Mervin C. Yoder, Principal Investigator, D. Ingram, Co-Principal Investigator, Effort 5%
- "The Role of Schwann Cell-Mast Cell Interactions in Neurofibroma Formation", Department of Defense (DOD), DAMD17-03-1-0216, 7/1/03—6/30/07, Annual Direct Cost \$810,837, D. W. Clapp, Principal Investigator, D. Ingram, Co-Principal Investigator, Effort 2%
- "Neurofibromatosis Type 1 Gene Regulates Myelopoiesis", National Institutes of Health (NIH), 2 R01 CA74177-06, 7/1/02—6/30/07, Annual Direct Cost \$250,000, D. W. Clapp, Principal Investigator, D. Ingram, Co-Principal Investigator, Effort 2%
- "Gene Therapy of X-linked Chronic Granulomatous Disease", NIH Program Project Grant – Project 2, 2 P01 HL053586-11A1, 7/1/05 – 6/30/10, Annual Direct Cost \$250,000, Mary C. Dinauer, Principal Investigator, D. Ingram, Co-Principal Investigator, Effort 5%

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Reuben Kapur	POSITION TITLE Assistant Professor of Pediatrics, Molecular Biology and Biochemistry		
eRA COMMONS USER NAME RKAPUR#a54321!			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Christ Church College, Kanpur, India	B.S.	1985	Physics, Chemistry,
Washington State University, Pullman, WA	B.S (cum	1989	Microbiology and
University of Arizona, Tucson, AZ	PhD	1994	Micro/Immunology Mol.

**A. Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

1989	Elected Phi Beta Kappa Society, Washing State University
1989	Elected Golden Key Honor Society, Washing State University
1989	First in graduating class, Washington State University
1989-1990	Graduate Academic fellowship, University of Arizona
1991-1992	Nominated Outstanding Instructor, University of Arizona
1994-1997	Howard Hughes postdoctoral fellowship, Indiana University School of Medicine
1997-1998	Leukemia Research foundation fellowship, Indiana University School of Medicine
1998-1999	NIH postdoctoral fellowship (NSRA), Indiana University School of Medicine
1997-1999	National Institute of Health (NIH) grant (NRSA F32 DK09752)
2000-2002	American Society of Hematology (ASH) Junior Faculty Scholar Award
2001-	Assistant Professor of Pediatrics, Molecular Biology and Biochemistry

**B. Selected peer-reviewed publications (in chronological order).**

- Harris, D.T., ***Kapur, R.***, Frye, C., Acevedo, A., Camenishch, T., Jaso-Friedmann, L., and D.L. Evans. A species-conserved NK cell antigen receptor is a novel vimentin-like molecule. ***Developmental and Comparative Immunology*, 16(5):395-403, 1992.**
- Kapur, R.***, Evans, D., and D.T. Harris. Evolutionary conservation of human function-associated molecule on murine natural killer cells: expression and function, ***Scandinavian Journal of Immunology*, 40(1):50-56, 1994.**
- Kapur, R.***, Evans, D. and D.T. Harris. An evolutionary conserved target cell antigen along with MHC class I molecules influences susceptibility to murine NK cell lysis. ***Developmental and Comparative Immunology*, 19(4):347-355, 1995.**
- Majumdar, M. K., Everett, E.T., Xiao, X., Cooper, R., Langley, K., ***Kapur, R.***, Vik, T., and D. A. Williams. Xenogeneic expression of human stem cell factor in transgenic mice mimics codominant c-kit mutations. ***Blood*, 87(8):3203-3211, 1996.**
- Kapur, R.***, Everett, E.T., Uffman, J., McAndrews-Hill, M., Cooper, R., Ryder, J., Vik, T., and D. A. Williams. Overexpression of human stem cell factor impairs melanocyte, mast cell, and thymocyte development: a role for receptor tyrosine kinase mediated MAP kinase activation in cell differentiation, ***Blood*, 90(8):3018-3026, 1997.**
- Maze, R., ***Kapur, R.***, Kelley, M.R., Hansen, W.K., Oh, S.Y., and D. A. Williams. Reversal of 1,3-bis(2-chloroethyl)-1-nitrosourea-induced severe immunodeficiency by transduction of murine long-lived hemopoietic progenitor cells using O6-methylguanine-DNA-methyltransferase cDNA. ***Journal of Immunology*, 158(2):1006-1013, 1997.**

7. **Kapur, R.** Majumdar, M. K., Xiao, X., Schindler, K., McAndrews-Hill, M., and D. A. Williams. Signaling through the interaction of membrane-restricted stem cell factor and c-kit receptor tyrosine kinase: genetic evidence for a differential role in erythropoiesis, ***Blood*, 91(3):879-889, 1998.**
8. Roberts, A.W., Kim, C., Zhen, L., Lowe, J.B., **Kapur, R.**, Petryniak, B., Spaetti, A., Pollock, J., Borneo, J.B., Bradford, G.B., Atkinson, S.J., Dinauer, M.C., and D.A. Williams. Deficiency of the hematopoietic cell-specific Rho-family GTPase, Rac2 is characterized by abnormalities in neutrophil function and host defense. ***Immunity*, 10(2):183-196, 1999.**
9. **Kapur, R.**, Cooper, R., Xiao, X., Donovan, P., Weiss, M., and D.A. Williams. The presence of novel amino acids in the cytoplasmic domain of stem cell factor results in hematopoietic defects in *Steel*<sup>17H</sup> mice. ***Blood*, 94(6):1915-1925, 1999.**
10. Yang, F.C., **Kapur, R.**, King, A.J., Tao, W., Kim, C., Borneo, J., Breese, R., Marshall, M., Dinauer, M.C., and D.A. Williams. Rac2 stimulates Akt activation affecting BAD/Bcl-xL expression while mediating survival and actin function in primary mast cells. ***Immunity*, 12(5):557-568, 2000.**
11. **Kapur, R.**, Cooper, R., Zhang, L., and D.A. Williams. Cross-talk between VLA-4/VLA-5 and c-Kit results in opposing effect on growth and survival of hematopoietic cells via the activation of focal adhesion kinase, mitogen-activated protein kinase, and Akt signaling pathways. ***Blood*, 97(7):1975-1981, 2001.**
12. **Kapur, R.**, and L. Zhang. A novel mechanism of cooperation between c-Kit and Epo-R. Stem cell factor induces the expression of Stat5 and Epo-R, resulting in efficient proliferation and survival by Epo. ***Journal of Biological Chemistry*, 276(2):1099-1106, 2001.**
13. Marques, S.A., Dy, L.C., Southhall, M.D., Yi, Q., Smietana, E., **Kapur, R.**, Marques, M., Travers, J.B., and D.F. Spandau. The platelet-activating factor receptor activates the extracellular signal-regulated kinase mitogen-activated protein kinase and induces proliferation of epidermal cells through an epidermal growth factor-receptor dependent pathway. ***The Journal of Pharmacology and Experimental Therapeutics*, 300(3):1026-1036, 2002.**
14. **Kapur, R.**, Chandra, S.C., Cooper, R., McCarthy, J., and D.A. Williams. Role of p38 and ERK MAP-Kinase in proliferation of erythroid progenitors in response to stimulation by soluble and membrane isoforms of stem cell factor. ***Blood*, 100(4):1287-1293, 2002.**
15. Ingram, D., Zhang, L., McCarthy, J., Wenning, M.J., Fisher, L., Yang, F.C., Clapp, D.W., and **R. Kapur.** Lymphoproliferative defects in mice lacking the expression of neurofibromin: functional and biochemical consequences of Nf1 deficiency in T-cell development and function. ***Blood*, 100(10):3656-3662, 2002.**
16. Xie, X., Chan, R.J., Johnson, S.A., Starr, M., McCarthy, J., **Kapur, R.**, and M.C. Yoder. Thrombopoietin promotes mixed lineage and megakaryocytic colony-forming cell growth but inhibits primitive and definitive erythropoiesis in cells isolated from each murine yolk sac. ***Blood*, 101(4):1329-1335, 2003.**
17. Tan, B.L., Yazicioglu, M.N., Ingram, D., McCarthy, J., Borneo, J., Williams, D.A., and **R. Kapur.** Genetic evidence for convergence of c-Kit- and alpha4 integrin-mediated signals on class IA PI-3kinase and the Rac pathway in regulating integrin-directed migration in mast cells. ***Blood*, 101(12):4725-4732, 2003.**
18. Tan, B.L., Hong, L., Munugalavadla, V., and **R. Kapur.** Functional and biochemical consequences of abrogating the activation of multiple diverse early signaling pathways in Kit. Role for Src kinase pathway in Kit-induced cooperation with erythropoietin receptor. ***Journal of Biological Chemistry*, 278(13):11686-11695, 2003.**
19. Huddleston, H., Tan, B., Yang, F.C., White, H., Wenning, M.J., Orazi, A., Yoder, M.C., **Kapur, R.**, and Ingram, D.A. Functional p85alpha gene is required for normal murine fetal erythropoiesis. ***Blood*, 102(1):142-145, 2003.**
20. Chandra, S., **Kapur, R.**, Chuzhanova, N., Summey, V., Prentice, D., Barker, J., Cooper, D.N. and D.A. Williams. A rare complex DNA rearrangement in the murine Steel gene results in exon duplication and a lethal phenotype. ***Blood*, 102(10):3548-3555, 2003.**
21. Ingram, D. A., Yang, F.C., Chen, S., Ratner, N., Monk, K.R., Clegg, T., White, H., Mead, L., Wenning, M.J., Williams, D.A., Atkinson, S., **Kapur, R.**, and D.W. Clapp. Neurofibromin-deficient Schwann cells secrete a potent migratory stimulus for Nf1<sup>+/-</sup> mast cells. ***Journal of Clinical Investigation*, 112(12):1851-1861, 2003.**

22. Hiatt, K., Ingram, D.A., Huddleston, H., Spandau, D.F., **Kapur, R.**, and D.W. Clapp. Loss of Nf1 tumor suppressor gene decreases fas antigen expression in myeloid cells. ***American Journal of Pathology*, 164(4):1471-1479, 2004.**
23. Hong, L., Munugalavadla, V., and **R. Kapur**. c-Kit-mediated overlapping and unique functional and biochemical outcomes via diverse signaling pathways, ***Molecular and Cellular Biology*, 24(3):1401-1410, 2004.**
24. Chan, R. J., Leedy, M. B., Munugalavadla, V., Voorhorst, C. S., Li, Y., Yu, M., and **Kapur, R.** Human somatic *PTPN11* mutations induce hematopoietic cell hypersensitivity to granulocyte-macrophage colony stimulating factor. ***Blood*, 105(9):3737-42, 2005.**
25. Khalaf, W. F., White, H., Wenning, M. J., Orazi, A., **Kapur, R.**, and Ingram, D. A. *K-Ras* is essential for normal fetal liver erythropoiesis. ***Blood*, 105(9):3538-41, 2005.**
26. Munugalavadla, V., and **Kapur, R.** Role of c-Kit and erythropoietin receptor in erythropoiesis. ***Critical Reviews in Oncology/Hematology*, 54(1):63-75, 2005.**
27. Munugalavadla, V., Ingram, D., and **Kapur, R.** p85 Subunit of Class IA PI-3Kinase plays an essential role in regulating growth and Actin based functions in macrophages. ***Blood, in press, 2005.***
28. Munugalavadla, V., Dore, L.C., Tan, B.L., Hong, L., Vishnu, M., Weiss, M.J., and **Kapur, R.** Repression of c-Kit and its Downstream Substrates by GATA-1 Inhibits Cell Proliferation During Erythroid Maturation, ***Molecular and Cellular Biology, in press, 2005.***

**C. Research Support.** List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

**Ongoing:**

NIH R01 HL 075816 (P.I. Kapur) "Mechanisms of adhesion and growth control in stem cells." The goal of this project is to determine the role of signaling molecules in stem cell adhesion, migration and growth. *January 1, 2004 – December 31, 2007.*

**Completed:**

American Society of Hematology Junior Faculty Scholar Award "Functional and biochemical analysis of adhesion induced "cross-talk" between c-Kit and integrins" *2000-2002.*

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed for Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

<b>NAME</b>		<b>POSITION TITLE</b>	
Patrick J. Loehrer, Sr., M.D.		Professor of Medicine	
<b>EDUCATION/TRAINING</b> (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
<b>INSTITUTION AND LOCATION</b>	<b>DEGREE</b> (if applicable)	<b>YEAR(s)</b>	<b>FIELD OF STUDY</b>
Purdue University, West Lafayette, Indiana	B.S.	1975	Mech Eng
Rush Medical College, Chicago, Illinois	M.D.	1978	Medicine

**A. Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

1978 - 1981 Internal Medicine Internship/Residency; Rush-Presbyterian St. Luke's Medical Center; Chicago, Illinois

1981 Assistant Professor of Medicine, Department of Internal Medicine, Rush-Presbyterian St. Luke's Medical Center; Chicago, Illinois

1981 - 1983 Oncology Fellowship, Indiana University Medical Center; Indianapolis, Indiana

1983 - 1988 Assistant Professor of Medicine, Department of Medicine, Section of Hematology/Oncology, Indiana University; Indianapolis, Indiana

1988 - 1993 Associate Professor of Medicine, Department of Medicine, Section of Hematology/Oncology, Indiana University; Indianapolis, Indiana University

1993 - Present Professor of Medicine, Department of Medicine, Section of Hematology/Oncology, Indiana University; Indianapolis, Indiana

2002- Present Director, Section of Hematology-Oncology, Indiana University

2002- Present Associate Director of Clinical Research, Indiana University Cancer Center

2005- Present Medical Director, Indiana University Cancer Hospital

**Post-graduate:**

1978 - 1980 Outstanding Resident

1980 Flick Family Fund Award

1981 - 1983 American Cancer Society Fellow

1983 - 1986 American Cancer Society Junior Faculty Fellow

1991 Glenn Irwin Jr., MD Experience Excellence Recognition Award

1999 Danielson Family Clinical Cancer Research Award

2000 Walther Cancer Institute Collaborator of the Year Award

2003 W. George Pinell Award

2004 Foundation for Thymic Research - Exceptional Service Award

2004 AOA

**Professional Activities (selected):**

1986 - Present Hoosier Oncology Group- Co-Founder, Chairman

1994 - Present Eastern Cooperative Oncology Group- Principal Investigator (IUMC)

1998 - 2001 American Society of Clinical Oncology, Board of Directors

2002 NIH State-of-the Science Panel: Endoscopic Retrograde  
Cholangiopancreatography  
2002- Present American Board of Internal Medicine: Board of Directors and Chair of Oncology  
Subspecialty Board

**Editorial Boards (selected):**

Oncology: International Journal of Cancer Research and Treatment  
Clinical Cancer Research  
Yearbook of Medicine (Co-Editor)  
Year Book of Oncology (Editor in Chief)

**B. Selected peer-reviewed publications (in chronological order).** Do not include publications submitted or in preparation.

1. Ulbright TM, **Loehrer PJ**, Roth LM, Einhorn LH, Williams SD, Clark SA: The Development of Non-Germ Cell Malignancies Within Germ Cell Tumors: A Clinicopathological Study of Eleven Cases. *Cancer* 54:1824-1933, 1984.
2. **Loehrer PJ**, Einhorn LH: Drugs Five Years Later...Cisplatin. *Ann Int Med* 100:704-713, 1984.
3. **Loehrer PJ**, Bonomi P, Goldman S, Reddy S, Gould V, Faber LP, Jensik R: Remission of Invasive Thymoma Due to Chemotherapy. *Chest* 87:377-380, 1985.
4. **Loehrer PJ**, Perez C, Roth LM, Greco FA, Livingston R: Chemotherapy for Advanced Thymoma: Preliminary Results. *Ann Int Med* 113:520-524, 1990.
5. **Loehrer PJ**, Einhorn LH, Williams SD: VP-16 plus Ifosfamide plus Cisplatin (VIP) as Salvage Therapy in Refractory Testicular Cancer. *J Clin Oncol* 4:528-536, 1986.
6. **Loehrer PJ**, Einhorn LH, Elson PJ, Crawford ED, Kuebler P, Tannock I, Raghavan D, Stuart-Harris R, Sarosdy MF, Lowe BA, Blumenstein B, Trump D: A Randomized Comparison of Cisplatin Alone or in Combination with Methotrexate, Vinblastine and Doxorubicin in Patients with Metastatic Urothelial Carcinoma: A Cooperative Group Study. *J Clin Oncol* 10:1066-1073, 1992.
7. **Loehrer PJ**, Johnson D, Elson P, Einhorn LH, Trump D: The Importance of Bleomycin in Favorable-Prognosis Disseminated Germ Cell Tumors: An Eastern Cooperative Group Trial. *J Clin Oncol* 13:470-76, 1995.
8. **Loehrer PJ**, Chen M, Kim KM, Aisner SC, Einhorn LH, Livingston R, Johnson D: Cisplatin, Doxorubicin and Cyclophosphamide plus Radiation Therapy for Limited Stage, Unresectable Thymoma: An Intergroup Trial. *J Clin Oncol* 15:3093-3099, 1997.
9. **Loehrer PJ**, Kim K, Aisner SC, Livingston R, Einhorn LH, Johnson D, Blum R: Cisplatin plus Doxorubicin plus Cyclophosphamide in Metastatic or Recurrent Thymoma: Final Results of an Intergroup Trial. *J Clin Oncol* 12: 1164-1168, 1994.
10. Thomas CR, Wright CD, **Loehrer PJ**: Thymoma: State of the Art. *J Clin Oncol* 17:2280-89, 1999.
11. **Loehrer PJ**, Gonin R, Nichols CR, Weathers T, Einhorn LH: Vinblastine plus Ifosfamide plus Cisplatin as Initial Salvage Therapy in Recurrent Germ Cell Tumors. *J Clin Oncol* 16: 2500-2504, 1998.
12. Henley, JD, Koukoulis GK, **Loehrer PJ**: Epidermal Growth Factor Receptor Expression in Invasive Thymoma. *Journal of Cancer Research and Clinical Oncology*, 2000
13. **Loehrer PJ**, Jiroutek M, Green M, Aisner J, Thomas CR, Livingston R, Johnson DH: Combined Etoposide, Ifosfamide, and Cisplatin in the Treatment of Patients with Advanced Thymoma and Thymic Carcinoma: An Intergroup Trial. *Cancer* 91:2010-2015, 2001.
14. Hanna N, Gharpure V, Cornetta K, Abonour R, Hromas R, **Loehrer PJ**: Phase II study of high dose carboplatin (C) with etoposide (E) in patients with recurrent thymoma. *Bone Marrow Transplantation*, 28 (5):435-438, 2001.
15. **Loehrer PJ**, Wang W, Johnson DH, Aisner S, Ettinger DS: Octreotide Alone or With Prednisone in Patients With Advanced Thymoma and Thymic Carcinoma: An Eastern Cooperative Oncology Group Phase II Trial. *Journal of Clinical Oncology* 22(2):293-299, 2004.
16. Kesler KA, **Loehrer PJ**: Thymoma: Current Medical and Surgical Management. *Seminars in Neurology*, 24(1):47-57, 2004

**C. Research Support.** List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and responsibilities of principal investigator identified above.

- 1) (Loehrer, Patrick J.) 01/01/86 - 06/30/00  
Walther Cancer Institute  
Hoosier Oncology Group

The Hoosier Oncology Group is a program of the Walther Cancer Institute

- 2) 5 U10 CA 49883-14 (Loehrer, Patrick) 07/01/94 - 04/30/04  
NIH/NCI  
Eastern Cooperative Oncology Group

The major goal of this project is to support the infrastructure of the conduct of ECOG-sponsored clinical trials.

- 3) 157-001 (Loehrer, Patrick J.) 07/28/97-07/25/03  
Glaxo Wellcome  
A Prospective, Randomized, Multicenter Phase II Clinical Trial Comparing the Effects of Panorex (17-1A Monoclonal Antibody) Injection plus 5-Fluorouracil-based Chemotherapy versus 5-FU-based Chemotherapy Alone.

The primary objective of this project is to compare the overall survival of patients with surgically resected stage III adenocarcinoma of the colon when treated with PANOREX injection in combination with 5-fu based chemotherapy vs. 5-FU based chemotherapy alone.

- 4) (Loehrer, Patrick J.) 07/01/99-06/30/03  
Frontier Science & Tech Res Fdn  
ECOG Outreach Program

The major goal of this project is to support the administrative coordination of affiliate participation in ECOG sponsored clinical trials.

- 5) 10030010/T98-1274 (Loehrer, Patrick J.) 05/10/99-08/09/02  
Taiho Pharmaceutical Company  
Joint USA/Japan Study of Oral Uracil/Ftorafur (UFT) plus Leucovorin in Patients with Metastatic Colorectal Carcinoma

The major goal of this project is to collaborate with Japanese doctors to test a GI cancer treatment.

- 6) LTS 7072A/-171 (Loehrer, Patrick J.) 05/15/00-12/31/02  
Sanofi-Synth Pharmaceuticals  
Compassionate Use Study of Oxaliplatin for Previously Treated Colorectal Cancer Patients.

The primary objective of this project is to provide oxaliplatin for compassionate use in patients who have received at least one prior chemotherapy regimen for locally advanced or metastatic colorectal cancer who are not eligible for standard therapies.

- 7) CP02-0141 (Loehrer, Patrick J.) 6/6/01-5/15/03  
Imclone Systems, Inc.  
Phase II Study of an Anti-Epidermal Growth Factor Receptor (EGFR) Antibody, Cetuximab, in Patients with Irinotecan-Refractory, Stage IV Colorectal Carcinoma

The main objective of this study is to evaluate the control of tumors and how long the tumor responds to Cetuximab.

- 8) CP02-0038 (Loehrer, Patrick J.) 9/25/01-9/24/03  
Imclone Systems, Inc.  
Pilot Study of an Anti-Epidermal Growth Factor Receptor (EGFR) Antibody, Cetuximab, in Combination with Irinotecan, Leucovorin, and Fluorouracil in Patients with Stage IV Colorectal Carcinoma.
- 9) (Loehrer, Patrick J.) 7/13/99 – 12/31/02  
Northwestern University  
A Phase I study of Docetaxel plus 5-FU, Cisplatin, and Leucovorin in Patients with Advanced Solid Tumors

The objectives of this study are to determine the maximally tolerated doses of docetaxel that can be given with cisplatin, 5-Fu and leucovorin, to identify the toxicities associated with combined chemotherapy using docetaxel, cisplatin, 5-fu and leucovorin and to evaluate the clinical response to the combined chemotherapy regimen in patients with advanced solid tumors.

- 10) NQ8-00-002 (Loehrer, Patrick J.) 3/21/01 – 9/30/03  
University of Arizona  
A Phase II Open Label Trial of Intravenous Gemcitabine with Oral Celecoxib in Patients with Locally Advanced or Metastatic Pancreatic Cancer

The main object of this study is to evaluate Gemcitabine plus Cox-2 inhibitor for the treatment of pancreatic cancer.

- 11) B9E-MC-JHFA (Loehrer, Patrick J.) 8/8/96 – 12/3/02  
Eli Lilly Corporation  
A Phase I study of Gemcitabine in Combination with Radiation Therapy in Patients with Localized, Unresectable Pancreatic Cancer

The main object of this study is to determine the MTD of the combination of gemcitabine and radiation therapy in the treatment of patients with locally advanced, unresectable pancreatic cancer.

- 12) (Loehrer, Patrick J.) 6/27/01 – 7/31/03  
Schering Corporation  
A Phase II Trial of Doxycycline and Interferon in Patients with Hepatocellular Carcinoma.

The main object of this study is to test a regimen of Doxycycline and Interferon in a clinical trial setting.

**BIOGRAPHICAL SKETCH**

NAME <b>Dr. Linda H. Malkas</b>	POSITION TITLE <b>Professor of Medicine</b>
eRA COMMONS USER NAME <b>Lmalkas</b>	<b>Vera Bradley Chair of Oncology</b>

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
City University of New York, NY	A.S.	1975	Engineering
City University of New York, NY	B.A	1977	Chemistry
City University of New York, NY	Ph.M.	1981	Biochemistry
City University of New York, NY	Ph.D.	1985	Biochemistry

**A. POSITIONS AND HONORS****Professional Experience:**

1987-1990 Postdoctoral Fellow, Worcester Foundation for Experimental Biology  
 1990-1995 Assistant Professor, University of Maryland School of Medicine, Department of Pharmacology  
 1995-2001 Associate Professor, University of Maryland School of Medicine, Department of Pharmacology  
 1999-2001 Affiliated Scientist, Los Alamos National Laboratory  
 2001-2002 Full Professor, University of Maryland School of Medicine, Department of Pharmacology  
 2002-present Full Professor, Indiana University School of Medicine, Department of Medicine  
 2002-present Vera Bradley Chair of Oncology  
 2002-present Co-leader of the Indiana University Cancer Center Breast Cancer Program  
 2003-present Director Vera Bradley Breast Cancer Research Program

**Awards and Recognition:**

1993-2005 NIH/NCI Public Health Service Award CA57350-09  
 1999-2005 NIH/NCI Public Health Service Award CA83199  
 1997-2000 NIH/NCI Public Health Service Award CA73060  
 1995-1997 NIH/NCI Shannon (Director's) Award  
 2005 Principal Speaker at the FASEB Research Conference on *Nuclear Structure and Cancer*  
 2004-present Editorial board member for the journal *Current Cancer Therapy Reviews*  
 2003-present Associate Editor – *Cancer Research*  
 2005 Principal Speaker at the FASEB Research Conference on *Nuclear Structure and Cancer*  
 2003 Breast Cancer Medical Researcher Award, Indiana Breast Cancer Alliance  
 2002 Plenary Speaker for INGEN Annual Proteomics Symposium  
 2001 Invited faculty for the *2<sup>nd</sup> Tumor Markers Conference*, MD Anderson Cancer Center  
 2001 Plenary Speaker at the FASEB Research Conference on *Nuclear Structure and Cancer*  
 1999 NIH *Chromatin, Transcription and DNA Replication Workshop* Plenary Speaker  
 1999 Chair & Speaker, *In Vitro DNA Replication Session*, Cell Proliferation Society Meeting  
 1998 Session Chair, *Cell Growth and Apoptosis*, Amer. Assoc. for Cancer Research Meeting  
 1996;1998;01 McGill University Conference *Regulation of Eukaryotic Replication* Plenary Speaker  
 1993 Session Chair, Gordon Research Conference on *Enzyme Organization and Cell Function*  
 1990-1991 Frank C. Bressler Research Fund Award  
 1986-1989 NIH Postdoc Fellowship, NCI

**Federal Government Advisory Committees:**

1994;1997-05 DOD Breast Cancer Program Study Section Member  
 1994-1998 NIH/NCI Study Section Member/Experimental Therapeutics I  
 1999;2003-04 DOD Ovarian Cancer Program Study Section Member  
 2000; 2002 NCI Site Visit Program Project Reviewer, Subcommittee D – Clinical Studies  
 2000; 2001 NCI Reviewer for Interdisciplinary Research Teams for Molecular Target Assessment  
 2001;2005 DOD Ovarian Cancer Program Grant Study Section Chair  
 2003-2008 NIH/NCI Cancer Molecular Pathobiology Study Section Member  
 2004;2005 NIH Reviewer for Academic Public Private Partnership Program Planning Grants  
 2004-present VA Merit Review Subcommittee for Oncology B – Full member

**B. RELEVANT PUBLICATIONS (from over 60)**

1. **Malkas, LH**, RJ Hickey, C Li and EF Baril (1990) A 21S enzyme complex from HeLa cells that functions in simian virus 40 DNA replication *in vitro*. *Biochemistry* 29:6362-6374.
2. Applegren, N, RJ Hickey, AM Kleinschmidt, Q Zhou, J Coll, P Wills, R Swaby, Y Wei, JY Quan, MYWT Lee and **LH Malkas** (1995) Characterization of the human cell multiprotein DNA replication complex. *J Cell Biochem* 59:91-107.
3. Tom TD, **LH Malkas** and RJ Hickey (1996) Identification of multiprotein complexes containing DNA replication factors by native immunoblotting of HeLa cell protein preparations with T-antigen-dependent SV40 DNA replication activity. *J Cell. Biochem.* 63: 259-267.
4. Coll, J, J Sekowski, L Schnaper, W Yue, A Brodie, RJ Hickey and **LH Malkas** (1996) Breast cell DNA synthesome: its purification from tumor tissue and cell culture. *Oncol. Res.* 8:435-447.
5. Lin, S, R Hickey and **L Malkas** (1997) A multiprotein DNA replication complex isolated from human leukemia cells is competent for DNA synthesis *in vitro*. *Leukemia Research* 21: 501-512.
6. Lin, S, R Hickey and **L Malkas** (1997) The biochemical status of the DNA synthesome can distinguish between permanent and temporary cell growth arrest. *Cell Grow. & Differ* 8: 1359-1369.
7. Coll, JM, RJ Hickey, EA Cronkey, H-Y Jiang, L Schnaper, MYWT Lee, L Uitto, JE Syvaaja, **LH Malkas** (1997) Mapping specific protein-protein interactions within the core component of the breast cell DNA synthesome. *Oncol. Res.* 9: 629-639.
8. Sekowski, JGW, **LH Malkas**, PE Bechtel, L Schnaper, and RJ Hickey (1998) Human breast cancer cells contain an error-prone DNA replication apparatus. *Cancer Research* 58: 3259-3263.
9. Bechtel, PE, RJ Hickey, L Schnaper & BJ Long, R Freund, N Liu, ME Smulson, C Rosenthal-Simbulan, JGW Sekowski, C Rodriguez-Valenzuela & **LH Malkas** (1998) Breast cells express an altered form of proliferating cell nuclear antigen (PCNA). *Cancer Research* 58: 3264-3269.
10. Simbulan-Rosenthal, CM, DS Rosenthal, A Hamid Boulares, R Hickey, **L Malkas**, J Coll and ME Smulson (1998) Regulation of the expression or recruitment of components of the DNA synthesome by poly(ADP-ribose) polymerase. *Biochemistry* 37: 9363-9370.
11. H. Pospiech, I. Kursula, W. Abdel-Aziz, **L. Malkas**, L. Uitto, M. Kastelli, M. Vihinen-Ranta, S. Eskelinen, and J.E. Syvaaja, (1999) A Neutralizing Antibody against Human DNA Polymerase  $\epsilon$  Inhibits Cellular but Not SV40 DNA Replication. *Nucl. Acids Res.* 27: 3799-3804.
12. D. Strumberg, A.A. Pilon, M. Smith, R. Hickey, **L. Malkas**, and Y. Pommier, Conversion of topoisomerase I cleavage complexes on the leading strand of ribosomal DNA into 5'-phosphorylated DNA double-stranded breaks by replication runoff. (2000) *Molecular and Cellular Biology* 20: 3977-3987.
13. **L. H. Malkas**, C. Langford, P. E. Bechtel, J. W. Sekowski, D. Tomic, L. Schnaper and D. Hoelz and R. J. Hickey, Cancer-Specific Form of Proliferating Cell Nuclear Antigen (csPCNA) is Present in Malignant Human Breast Cells and Tissues (2002) *J. Clinical Ligand Assay.* 25: No. 1, 20-32.
14. **L. H. Malkas**, C. Langford, D. Tomic, D. Hoelz, Liu, Y., L. Schnaper and R. J. Hickey (2002) Mining the cancer cell's DNA replication apparatus for new biomarkers and therapeutic targets. In: *Tumor Markers: Physiology, Pathobiology, Technology, and Clinical Applications*, AACR Press, 35: 411-421
15. Jiang, H., Hickey, R.J., Tom, T.D., Wills, P. W., Abdel-Aziz, W. F. and **Malkas, L.H.** (2002) DNA Replication Is Mediated By a Discrete Multiprotein Complex. *J. Cellular Biochemistry.* 85:762-774.
16. D. Tomic, S. G. Brodie, C. Deng, R. J. Hickey, J. K. Babus, **L. H. Malkas** and J. A. Flaws, Smad 3 May Regulate Follicular Growth in the Mouse Ovary. (2002) *Biology of Reproduction* 66: 917-923.
17. P. M. Vertino, J. A. Sekowski, J. M. Coll, N. Applegren, S. Han, R.J. Hickey and **L. H. Malkas**, DNMT1 is a component of a multiprotein DNA replication complex. (2002) *Cell Cycle* 6:416-423.
18. R. J. Hickey, D. Hoelz, **L. H. Malkas**, Eukaryotic DNA Replication. (2004) *Encycl. Life Sciences*, Nature Publ.
19. Waleed Abdel-Aziz, Robert J. Hickey, and **Linda H. Malkas**. An *in vitro* model system that can differentiate the stages of DNA replication affected by anticancer agents. (2004) *Biochemical Pharmacology* 68: 11-21.
20. J. Yang, Zhiwen Chen, Yang Liu, Robert J. Hickey, and **Linda H. Malkas**, Altered DNA Polymerase  $\alpha$  expression in Breast Cancer Cells Leads to a Reduction in DNA Replication Fidelity and a Higher Rate of Mutagenesis. (2004) *Cancer Research* 64: 5597-5607.
21. Mauricio A. Escobar\*, Derek J. Hoelz\*, John A. Sandoval, Robert J. Hickey, Jay L. Grosfeld and **Linda H. Malkas**, Profiling of Nuclear Extract Proteins From Human Neuroblastoma Cell Lines: The Search for Fingerprints, (2005) *Journal of Pediatric Surgery* 40:349-58. \* These authors contributed equally to the project.
22. Sandoval JA, Grosfeld JL, Hickey RJ, and **Malkas LH**. Structural Analysis of the Human Neuroblastoma DNA Replication Complex: Insights into Faulty Proliferation. (2005) *Journal of Pediatric Surgery* (in press).
23. Sandoval JA, Hoelz DJ, Woodruff HA, Powell RL, Jay CL, Grosfeld JL, Hickey RJ, and **Malkas LH**. Novel peptides secreted from human neuroblastoma: Useful clinical tools? (2005) *Journal of Pediatric Surgery* (in press).
24. Eppstein AC, Sandoval JA, Klein PJ, Woodruff HA, Grosfeld JL, Hickey RJ, **Malkas LH**, Schmidt CM. Differential Signaling Response of Neuroblastoma to MEK Activity Inhibitor Predicts Resistance to MAP Kinase Based Treatment Strategies. (2005) *Journal of Pediatric Surgery* (in press).

**C. RESEARCH SUPPORT**

**Center of Excellence (BC030400) Sledge (PI)**

**04/01/04-04/30/09**

**Department of Defense (DOD)**

“Center of Excellence for Individualization of Therapy for Breast Cancer” (The purpose of the Center of Excellence is to combine the emerging technologies of genomics, proteomics, and pharmacogenetics / pharmacogenomics to predict the response to commonly used chemotherapeutic agents and novel targeted agents in the setting of advanced breast cancer. The predicted outcome of such analyses will be therapeutic individualization, the matching of individual agents to specific patients most likely to benefit in the least toxic possible manner.) **Role:** Co-Leader

**DAMD17-02-1-0467**

**Hoelz (PI)**

**10/01/02-09/01/05**

**Department of Defense (DOD)**

“Cancer Specific Proliferating Cell Nuclear Antigen as a Novel Diagnostic Marker for the Detection of Breast Cancer.” (The goal of this research is to develop an enzyme linked immunsorbent assay (ELISA) that utilizes the 29 amino acid fragment of XPG to detect the presence of csPCNA in cells, tissues, and sera.) **Role:** Mentor/Co-Investigator

**P30 CA82709-06**

**Williams (PI)**

**09/01/01-08/31/09**

**NIH/NCI Cancer Center Support Grant**

The major goal of this project is to help support the research programs that have been established to allow successful collaboration among basic and clinical researchers. **Role:** Co-Program Leader-Breast Cancer Program

**COMPLETED:**

**RO1 (CA83199-06)**

**Malkas (PI)**

**07/01/99-06/30/04**

**NIH/NCI**

“Development and Evaluation of a Novel Cancer Biomarker.” (This project is aimed at the development and validation of an antibody directed specifically at a uniquely altered form of PCNA found in breast cancer cells.)

**Role:** PI

## BIOGRAPHICAL SKETCH

NAME	POSITION TITLE		
Keith L. March, MD, PhD	Professor of Medicine, Indiana University		
	Professor of Cellular & Integrative Physiology, Indiana University		
	Adjunct Professor of Biomedical Engineering, Purdue University		
	Director, Indiana Center for Vascular Biology & Medicine		
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
St. Francis College, Fort Wayne, IN	BS	1979	Biology/Chemistry
Indiana University, Bloomington, IN	PhD	1983	Biochemistry
Indiana University School of Medicine	MD	1985	Medicine
Indiana University School of Medicine		1988	Internal Medicine Residency
Indiana University School of Medicine		1990	Cardiology Clinical Fellowship

### Positions

1985 - 1988 Internship and Residency, Indiana University School of Medicine  
 1988 - 1990 Cardiology Fellowship, Indiana University Medical Center  
 1990 - 1995 Assistant Professor of Medicine, Indiana University Medical Center  
 1990 - present Research Associate, Krannert Institute of Cardiology  
 1995 - 2003 Associate Professor of Medicine, Indiana University Medical Center  
 1999 - 2003 Associate Professor of Cellular & Integrative Physiology, Indiana University Medical Center  
 1999 - 2/2002 Director, Indiana University MD/PhD Combined Degree Program  
 1999 - present Director, Indiana Center for Vascular Biology & Medicine  
 2002 Adjunct Associate Professor of Biomedical Engineering, Purdue University  
 2003 - present Professor of Medicine and Cellular & Integrative Physiology, Indiana University  
 Adjunct Professor of Biomedical Engineering, Purdue University  
 2004 - present Cryptic Masons Medical Research Foundation Professor of Vascular Biology Research

### Honors

1979 - 1985 Insurance Medical Scientist Scholarship  
 1981 Robert Chernin Award for Outstanding Graduate Research  
 1983 Alpha Omega Alpha Medical Honor Society  
 1983 Robert W. Bullard Outstanding Medical Science Student Award  
 1984 John H. Edwards Fellowship for Highest Distinction as Graduate Student  
 1989 USCI Cardiology Fellowship Award

### Selected Publications

- Sindermann JR, **March KL**. Heparin Responsiveness In Vitro As A Prognostic Tool For Vascular Graft Stenosis: A Tale Of Two Cell Types? *Circulation*. 1998 Jun 30; 97(25):2486-90.
- Stoll HP, Carlson K, Keefer LK, Hrabie JA, **March KL**. Pharmacokinetics And Consistency Of Pericardial Delivery Directed To Coronary Arteries: Direct Comparison With Endoluminal Delivery. *Clin Cardiol*. 1999 Jan; 22(1 Suppl 1):110-6.
- March KL**, Woody M, Mehdi K, Zipes DP, Brantly M, Trapnell BC. Efficient In Vivo Catheter-Based Pericardial Gene Transfer Mediated By Adenoviral Vectors. *Clin Cardiol*. 1999 Jan; 22(1 Suppl 1):I23-9.
- Dickson TJ, Gurudutt V, Nguyen AQ, Kumfer K, Maxted W, Brown J, Mahomed Y, Sharp T, Aufiero TX, Fineberg N, **March KL**. Establishment Of A Clinically Correlated Human Pericardial Fluid Bank: Evaluation Of Intrapericardial Diagnostic Potential. *Clin Cardiol*. 1999 Jan; 22(1 Suppl 1):I40-2.
- Kraemer R, Nguyen H, **March KL**, Hempstead B. NGF Activates Similar Intracellular Signaling Pathways In Vascular Smooth Muscle Cells As PDGF-BB But Elicits Different Biological Responses. *Arter Thromb Vasc Biol*. 1999 Apr; 19(4):1041-50.
- Wilensky RL, Mehdi K, Sowinski KM, Baek SH, **March KL**. Increased Intramural Retention after Local Delivery of Molecules with Increased Binding Properties: Implications for Regional Delivery of Pharmacologic Agents. *J Cardiovasc Pharmacol Ther*. 1999 Apr; 4(2):103-112.
- March KL**, Sandusky G, Fan L. Hyperplasia In Multiple Smooth Muscle Tissues In Transgenic Mice Expressing A Temperature-Sensitive SV40 T-Antigen Under The Control Of Smooth Muscle Alpha-Actin Regulatory Sequences. *Oncogene*. 1999 Jun 24; 18(25):3773-82.

8. Sindermann JR, Fan L, Weigel KA, Troyer D, Muller JG, Schmidt A, **March KL**, Breithardt G. Differences In The Effects Of HMG-Coa Reductase Inhibitors On Proliferation And Viability Of Smooth Muscle Cells In Culture. *Atherosclerosis*. 2000 Jun; 150(2):331-41.
9. Hou D, Rogers PI, Toleikis PM, Hunter W, **March KL**. Intrapericardial Paclitaxel Delivery Inhibits Neointimal Proliferation And Promotes Arterial Enlargement After Porcine Coronary Overstretch. *Circulation*. 2000 Sep 26; 102(13):1575-81.
10. Wang S, Bray P, McCaffrey T, **March KL**, Hempstead BL, Kraemer R. p75NTR Mediates Neurotrophin-Induced Apoptosis of Vascular Smooth Muscle Cells. *Am J Pathol*. 2000 Oct; 157: 1247-1258.
11. Stoll HP, Hutchins GD, Winkle WL, Nguyen AT, Hou D, Appledorn CR, Romeike B, **March KL**. Liquid-Filled Balloon Brachytherapy Using (68)Ga Is Effective And Safe Because Of The Short 68-Minute Half-Life: Results Of A Feasibility Study In The Porcine Coronary Overstretch Model. *Circulation*. 2001 Apr 3; 103(13):1793-8.
12. Stoll HP, Hutchins GD, Winkle WL, Nguyen AT, Appledorn CR, Janzen I, Seifert H, Rube C, Schieffer H, **March KL**. Advantages Of Short-Lived Positron-Emitting Radioisotopes For Intracoronary Radiation Therapy With Liquid-Filled Balloons To Prevent Restenosis. *J Nucl Med*. 2001 Sep; 42(9):1375-83.
13. Baek SH, Hrabie JA, Keefer LK, Hou DM, Fineberg N, Rhoades R, **March KL**. Augmentation of Intrapericardial Nitric Oxide (NO) Level by a Prolonged-Release NO Donor Reduces Luminal narrowing After Porcine Coronary Angioplasty. *Circulation*. 2002. Jun 11; 105(23):2779-84.
14. Sindermann JR, Smith J, Kobbert C, Plenz G, Skaletz-Rorowski A, Solomon JL, Fan L, **March KL**. Direct Evidence for the Importance of P130 in Injury Response and Arterial Remodeling Following Carotid Artery Ligation. *Cardiovasc Res*. 2002 Jun; 54(3):676-83.
15. Boekstegers P, Raake P, Al Ghobainy R, Horstkotte J, Hinkel R, Sandner T, Wichels R, Meisner F, Thein E, **March KL**, Boehm D, Reichenspurner H. Stent-Based Approach for Ventricle-to-Coronary Artery Bypass. *Circulation*. 2002 Aug; 106(8):1000-1006.
16. Sindermann JR, Babij P, Klink JC, Kobbert C, Plenz G, Ebbing J, Fan L, **March KL**. Smooth Muscle-Specific Expression of SV40 large TAg Induces SMC Proliferation Causing Adaptive Arterial Remodeling. *Amer J Phys Heart*. 2002 Dec; 283(6): H2714-24.
17. Hou DM, **March KL**. A Novel Percutaneous Technique for Accessing the Normal Pericardium: A Single-Center Successful Experience of 53 Porcine Procedures. *J. Invas Cardiol*. 2003 Jan; 15(1): 13-17.
18. Hou DM, Maclaughlin F, Thiesse M, Panchal VR, Bekkers SCAM, Wilson EA, Rogers PI, Coleman MC, **March KL**. Widespread Regional Myocardial Transfection by Plasmid Encoding Del-1 Following Retrograde Coronary Venous Delivery. *Cath and Card Interv*. 2003 Feb; 58(2): 207-211.
19. Rehman J, Li J, Orschell CM, **March KL**. Peripheral Blood "Endothelial Progenitor Cells" are Derived from Monocyte/Macrophages and Secrete Angiogenic Growth Factors. *Circulation*. 2003 March; 107:1164-1169.
20. Rehman J, Considine RV, Bovenkerk JE, Williams CA, Li J, Jones RM, **March KL**. Obesity is Associated with Increased Levels of Circulating Hepatocyte Growth Factor. *J Amer Col Card*. 2003 April; 41(8): 1408-1413.
21. Sindermann JR, Kobbert C, Bauer F, Skaletz-Rorowski A, Hohage H, Plenz G, Breithardt G, **March KL**. Vascular Ligation Response is Independent of p107: Stressing the Role of the Related p130. *Amer J Phys Heart*. 2003 Aug; 285(2): H915-918.
22. Rehman J, Traktuev D, Li J, Merfeld-Clauss S, Temm CJ, Bovenkerk JE, Pell C, Johnstone B, Considine RV, **March KL**. The Secretion of Angiogenic and Anti-Apoptotic Factors by Human Adipose Stromal Cells. *Circulation*. Mar 2004; 109(10): 1291-1298.
23. Panchal VR, Rehman J, Nguyen AT, **March KL**. Reduced Pericardial Levels of Endostatin Correlate with Collateral Development in Patients with Ischemic Heart Disease. *J Amer Col Card*. 43(8): 1383-1387.
24. Rehman J, Li J, Parvathaneni L, Karlsson G, Panchal VR, Temm CJ, Mahenthiran J, **March KL**. Exercise Acutely Increases Circulating Endothelial Progenitor Cells and Monocyte-/Macrophage-Derived Angiogenic Cells. *J Amer Col Card*. 2004 June 16; 43(12): 2314-2318.
25. **March KL**, Johnstone BH. Cellular approaches to tissue repair in cardiovascular disease: the more we know, the more there is to learn. *American Journal of Physiology. Heart and Circulatory Physiology*. Aug 2004. 287:H458-63.
26. Hou, D, Youssef EA, Brinton TJ, Zhang P, Rogers P, Price, ET, Yeung AC, Johnstone BH, Yock PG, **March KL**. Radiolabeled cell distribution after intramyocardial, intracoronary, and interstitial retrograde coronary venous delivery: Implications for current clinical trials. *Circulation*. 2005 August 30;112:1150-6.
27. Youssef EA, Zhang P, Rogers PI, Tremble P, Rokovich J, Johnstone BH, **March KL**, Hou, D, Enhancing myocardial plasmid expression by retrograde coronary venous delivery. *Catheter Cardiovasc Interv*. 2005 Aug; 65(4):528-34
28. Case, J, Horvath TL, Howell JC, Yoder MC, **March KL**, Srouf EF. Clonal multilineage differentiation of murine common pluripotent stem cells isolated from skeletal muscle and adipose stromal cells. *Ann N Y Acad Sci*. 2005 Jun; 1044:183-200.
29. Rehman J, **March KL**, Stem Cells and Progenitor Cells in Cardiovascular Disease. Textbook: Contemporary Cardiology: Principles of Molecular Cardiology, Humana Press Inc., Totowa, NJ 2005. pp.71-80 (2005).

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30. Sindermann JR, **March KL**. Balancing luminal size and smooth muscle proliferation—a key control point in atherosclerosis and arteriogenesis. *EXS*. 2005;(94):193-205.

#### **Book**

1. **March KL**, ed. *Gene Transfer in the Cardiovascular System: Experimental Approaches and Therapeutic Implications*. Boston: Kluwer Academic Publishers. 1997.

#### **Ongoing Research Support**

**National Institutes of Health, *Adipose Stromal Cells in Vascular Repair and Hematopoiesis***, 2004-2009, Principal Investigator. This grant evaluates and characterizes the role of cells found in adipose tissue in making or repairing blood vessel cells as well as in hematopoiesis. \$1,857,915

**National Institutes of Health. *Training Program in Vascular Biology and Medicine***, 2005-2010, Principal Investigator. This grant supports 5 post-doctoral fellows yearly for training in vascular biology, including stem cell biology. \$1,157,062.

**Veterans' Administration Merit Review Award. *Adipose Stromal Cells in Angiogenesis and Tissue Repair***, 2005-2009. Principal Investigator. This grant characterizes the role of adipose stromal cells in modifying vascular and tissue responses to vascular ischemic insult in skeletal and cardiac muscle. \$800,000.

**Biomet-Cell Factor Technologies, Inc.. *Phase I - Animal Research Study Agreement***. Phase I of a two phase study using the protocol entitled "Use of adipose stromal cells to promote wound repair in a porcine model of dermal wounding". 2005. Principal Investigator. The major goal of this project is to process fat and isolate stem cells. \$32,568.

**Biomet-Cell Factor Technologies, Inc.. *Phase II - Animal Research Study Agreement***. Phase II of a two phase study using the protocol entitled "Use of adipose stromal cells to promote wound repair in a porcine model of dermal wounding". 2005-2006. Principal Investigator. The major goal of this project is to demonstrate the potential of autologous adipose stromal cells for accelerating wound repair. \$67,179.

**Biomet-Cell Factor Technologies, Inc. *Stem Cell Mediated Angiogenesis Trial***. Clinical research study on the clinical effectiveness of bone marrow derived stem cells. 2005-2007. Co-Investigator (PI, Murphy). \$455,685.

**Cell Factor Technologies, Inc. *Animal Research Study Agreement: Phase I- Distribution and effect of stromal cells infused into an infarcted porcine heart; Phase II-determination of MTD; Phase III-determination of efficacy***. Study of effects of adipose stromal cells in the context of acute porcine myocardial infarction. 2005-2007. \$652,582.

**Aastrom Biosciences, Inc. *Clinical Protocol Evaluating TRC Bone Marrow Cells in Limb Ischemia***. 2005-2007. Co-Primary Investigator (Co-PI, Murphy). \$541,379

**Johnson and Johnson - Center for Biomaterials & Advanced Technologies. *Cell delivery to promote reperfusion in a mouse ischemic Hindlimb Model***. This study demonstrates the potential of a cell therapy for re-establishing flow of blood in a model of critical limb ischemia. 2005-2006. \$68,500.

**Eli Lilly & Company, Inc., *Utilizing the Multipotency of Human Adipose Stromal Cells***, 2003-2005, Principal Investigator. The major goal of this project is to define the characteristics of fat-derived stromal cells. \$237,139.

**Venomatrix, *Interstitial Retrograde Venous Cell Delivery***, 2003-2005. Principal Investigator. The major goal of this project is to optimize a novel catheter device for agent delivery to the heart. \$214,465.

**Medtronic, Inc. *Intrapericardial Delivery Of Nitric Oxide To Induce Angiogenesis In The Hypercholesterolemic Pig Coronary Ischemic Model***, 2004-2006, Co-Investigator (PI, Hou). The major goal of this project is to study relating to intrapericardial delivery of nitric oxide to induce angiogenesis to treat coronary artery disease. \$176,724

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### **Completed Research Support, recent**

National Institutes of Health (R01), *Smooth Muscle Diversity and Cell Cycle Control*, 1997-2002, Principal Investigator. This grant evaluates smooth muscle cell cycling in transgenic animal models.

Veteran's Administration Merit Review Award, *Vascular Smooth Muscle Immortalization and Cell Cycle Control*, 1997-2000, Principal Investigator. This grant supported transgenic mouse modeling of vascular disease

Veteran's Administration Merit Review Award, *Molecular Mechanisms Directing Artery Remodeling*, 2000 – 2005, Principal Investigator. This grant evaluates mechanisms of large artery remodeling. \$800,000.

National Institutes of Health (SBIR), *Ultrasound Assisted Transmural Drug Delivery*, 2000 – 2002, Principal Academic Investigator. This grant evaluated the effects of ultrasound on the artery wall.

National Institutes of Health (R21), *Non-Invasive Myocardial Revascularization Using Targeted Proton Beam Irradiation for Induction of Angiogenesis*, 1998-2002, Principal Investigator.

Pfizer, Inc., *Effects of Statins on Circulating Endothelial Progenitor Cells*, 2002 - 2004, Principal Investigator. This grant supported studies of endothelial progenitor cells.

Valentis, Inc., *Retrograde Coronary Delivery of Plasmids for Myocardial Angiogenesis*, 2000 – 2002, Principal Investigator. This grant evaluated the expression and efficacy of a del-1 plasmid administered into the heart.

Edwards Lifesciences, LLC, *Optimization of Gene Delivery in Rabbit Hind Limb and Porcine Ischemia Models*, 2003-2004, Principal Investigator. The major goal of this project was to evaluate a new category of proteins to regulate angiogenesis, in models of both heart and leg ischemia.

U.S. Civilian Research & Development Foundation, *Angiogenesis Control by the Urokinase System: Biochemical Mechanisms and Gene Therapy Approaches to Ischemia*, 2003-2005, Principal Investigator. This grant involves the molecular mechanisms of urokinase effects on angiogenesis. \$11,208.

Principal Investigator/Program Director (Last, first, middle):

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**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed for Form Page 2.  
Follow the sample format for each person. **DO NOT EXCEED FOUR PAGES.**

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NAME	POSITION TITLE
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EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY

Principal Investigator/Program Director (Last, First, Middle):

Principal Investigator/Program Director (Last, First, Middle):

Principal Investigator/Program Director (Last, First, Middle):

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Harikrishna Nakshatri	POSITION TITLE Associate Professor, Department of Surgery, Biochemistry and Molecular Biology Marian J. Morrison Investigator in Breast Cancer		
eRA COMMONS USER NAME hnakshat			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University of Agricultural Sciences, Bangalore,	B.V.Sc.	1977-1982	Veterinary Medicine
Memorial University of Newfoundland, St. John's,	Ph.D.	1986-1990	Molecular Biology
LGME, University Louis Pasteur, Strasbourg,	Post-doc	1990-1993	Molecular Biology
Picower Institute for Medical Research, New	Investigator	1993-1995	Molecular Biology

**A. Positions and Honors****Positions**

- 1996-2002 Assistant Professor, Indiana University School of Medicine, Indianapolis, Indiana.  
1997- Member, Walther Oncology Center, Indiana University School of Medicine  
2000- Adjunct Faculty, Veterinary Clinical Sciences, Purdue University, Indiana  
2002- Associate Professor, Indiana University School of Medicine  
2004- Marian J. Morrison Investigator in Breast Cancer Research, Indiana University

**Honors**

- 1977-1982: Indian Council of Agricultural Research Student-ship.  
1982 Three gold medals and one state award for obtaining top rank in Veterinary Science  
1988 The Cancer Research Society Inc., Quebec, Canada fellowship  
1988 Excellence in Research Award, Memorial University of Newfoundland.  
1989-1990 The National Cancer Institute of Canada fellowship  
1989 Colman graduate student award, Memorial University of Newfoundland.  
2002 International Cancer Congress Travel Award, American Cancer Society  
2002 Inaugural Michael K. Guest Award for Innovative Research by Walther Cancer Institute  
2005 US patent # 6,890,946 Use of parthenolide to inhibit cancer

**Professional Activities**

- Florida Department of Health Biomedical Research Program (2001, 2003, 2004)  
Department of Defense (US army) Ovarian Cancer Review Panel (2001)  
Guy's and St. Thomas Charitable Foundation, London, UK (2002)  
Department of Defense Breast Cancer Concept Award review panel (2003)  
National Institutes of Environmental Health Sciences Special Emphasis Panel (July, 2003).  
The Canadian Institutes of Health Research Grant Review (2004)  
NRSA fellowship study section, NIH (2004 - 2005)  
Department of Health, Pennsylvania (2004)  
Ad Hoc Review, MCE Study Section – NIH (2005)

**B. Selected peer-reviewed publications (in chronological order, out of 56).**

32. Shinichi Nozaki, George W. Sledge, Jr., and **Harikrishna Nakshatri (2000)** Cancer Cell-derived interleukin 1-alpha contributes to autocrine and paracrine induction of pro-metastatic genes in breast cancer. *Biochem. Biophys. Res. Commun* 275: 60-62.  
35. Robert A. Campbell, Poornima Bhat-Nakshatri, Nikhil M. Patel, Demetra Constantinidou, Simak Ali, and **Harikrishna Nakshatri (2001)** PI3 kinase/AKT-mediated activation of estrogen receptor alpha: a new model for anti-estrogen resistance. *J. Biol. Chem.* 276:9817-9824.

36. Shinichi Nozaki, George W. Sledge and **Harikrishna Nakshatri (2001)** Repression of GADD153/CHOP by NF-Kappa-B: a possible cellular defense against endoplasmic reticulum stress-induced cell death. *Oncogene* 20:2178-2185.
41. Poornima Bhat-Nakshatri, Christopher J. Sweeney, and **Harikrishna Nakshatri (2002)** Identification of signal transduction pathways involved in constitutive NF-Kappa-B activation in breast cancer cells. *Oncogene* 21: 2066-2078.
42. **Harikrishna Nakshatri** and Robert Goulet **(2002)** NF-Kappa-B and Breast cancer. *Current Problems in Cancer* 26:282-309
43. Helbig, G., Christopherson, K. W., Bhat-Nakshatri, P., Kumar, S., Miller, K. D., Broxmeyer, H. E. and **H. Nakshatri (2003)** NF- $\kappa$ B promotes breast cancer cell migration and metastasis by inducing the expression of the chemokine receptor CXCR4. *J. Biol. Chem.* 278:21631-21638.
44. Suresh Kumar, Hiromitsu Kishimoto, Hui Lin Chua, Sunil Badve, Kathy D. Miller, Robert M. Bigsby, and **Harikrishna Nakshatri (2003)** Interleukin 1 $\beta$  Promotes Tumor Growth and Cachexia in MCF-7 Xenograft Model of Breast Cancer. *American Journal of Pathology* 163:2531-2541.
45. P. Bhat-Nakshatri, R.A. Campbell, N.M. Patel, T.R. Newton, AJ. King, M.S. Marshall, S. Ali, and **H. Nakshatri (2004)** Tumor necrosis factor and PI3-kinase control estrogen receptor alpha protein level and its transrepression function. *British Journal of Cancer* 90:853-859.
46. Curry III EA, Murry D. J., Yoder C., Fife, K., Armstrong, V., **Nakshatri, H.**, O'Connell, M and Sweeney, CJ. **(2004)** Phase I dose escalation trial of feverfew with standardized doses of parthenolide in patients with cancer. *Invest New Drugs* 22:299-305.
47. Christopher Sweeney, Lang Li., Rajasubramaniam Shanmugam, Poornima Bhat-Nakshatri, Lee Ann Baldrige, Thomas Gardner, Martin Smith, Michael Koch, **Harikrishna Nakshatri** and Liang Cheng **(2004)** Nuclear Factor KappaB is constitutively activated in prostate cancer in vitro and is over-expressed in prostatic intra-epithelial neoplasia and adenocarcinoma of the prostate. *Clinical Cancer Research* 10:5501-5507.
48. **Harikrishna Nakshatri**, Susan P. Rice and Poornima Bhat-Nakshatri **(2004)** The Anti-tumor Agent Parthenolide Reverses Resistance of Breast Cancer Cells to Tumor Necrosis Factor-related Apoptosis-inducing Ligand Through Sustained Activation of c-Jun N-terminal Kinase. *Oncogene* 23:7330-7344.
49. Fan, M., **Nakshatri, H.**, and Nephew, K.P. **(2004)** Inhibiting proteosomal proteolysis sustains estrogen receptor-(alpha) activation. *Mol. Endocrinol.* 18:2603-2615.
50. Zhuo Wang, Hiromitsu Kishimoto, Poornima Bhat-Nakshatri, Colin Crean and **Harikrishna Nakshatri (2005)** TNF $\alpha$  resistance in MCF-7 breast cancer cells is associated with altered subcellular localization of p21<sup>CIP1</sup> and p27<sup>KIP1</sup>. *Cell Death and Differentiation* 12:98-100.
51. Wollmann W, Goodman ML, Bhat-Nakshatri P, Kishimoto H, Goulet RJ, Meharotra S, Morimiya A, Badve S, **Nakshatri H (2005)** The Macrophage Inhibitory Cytokine Integrates AKT/PKB and MAP Kinase Signaling Pathways in Breast Cancer Cells, *Carcinogenesis*, 26:900-907.
52. Yip-Schneider MT, **Nakshatri H**, Sweeney CJ, Marshall MS, Wiebke EA, Schmidt CM **(2005)** Parthenolide and Sulindac Cooperate to Mediate Growth Suppression and Inhibits the Nuclear Factor-kappa B Pathway in Pancreatic Carcinoma Cells, *Molecular Can Therapeutics*, 4:587-594.
53. Sweeney CJ, Mehrotra S, Sadaria MR, Kumar S, Shortle NH, Roman Y, Sheridan C, Campbell RA, Murray DJ, Badve S, **Nakshatri H (2005)** The Sesquiterpene Lactone Parthenolide in Combination with Docetaxel Reduces Metastasis and Improves Survival in a Xenograft Model of Breast Cancer. *Molecular Can Therapeutics* 4:1004-1112.
54. Wang Z, Goulet R, Stanton KJ, Sadaria M, **Nakshatri H (2005)** Differential Effect of Anti-apoptotic Genes Bcl-xL and c-FLIP on Sensitivity of MCF-7 Breast Cancer Cells to Paclitaxel and Docetaxel, *AntiCancer Research*, 24: 2367-2380
55. Hiromitsu Kishimoto, Zhuo Wang, Poornima Bhat-Nakshatri, David Chang, Robert Clarke and **Harikrishna Nakshatri (2005)** The p150 family co-activators regulate breast cancer cell proliferation and invasion through autocrine/paracrine activity of SDF-1 $\alpha$ /CXCL12. *Carcinogenesis* (In press).
56. **Harikrishna Nakshatri (2005)** Weapons for selective cancer destruction: Death receptors in cancer therapy (Book review), *Leukemia Research*, (In press).

## C. Research Support

### **ON-GOING**

R01-CA89153 (Nakshatri, H) 05/01/2001 to 04/30/2006

NIH/NCI

“AKT-mediated tamoxifen resistance in breast cancer”

The major goal of this study is to determine whether serine/threonine kinase AKT mediated tamoxifen resistance in breast cancer cells is Estrogen receptor dependent.

00A069-REN (Nakshatri, H) 07/01/2003 to 06/30/2006 (On- One Year Cost Extension)

American Institute for Cancer Research

“The Role of the Herb Feverfew in Preventing CXCR-4 Mediated Metastasis of Breast Cancer”

The major goal of this study is to determine whether treatment with parthenolide and apigenin reduces metastasis and enhances survival.

Kentucky Lung Cancer Program (Crooks, P.) 01/01/2004 to 12/31/2005

Parthenolides as Potential Treatments for Lung Cancer

The major objective of this project is to determine the effect of parthenolide and its analogues on growth of lung cancer xenografts.

Co-Investigator – H. Nakshatri, PhD

Collaboration in Biomedical research grant (IUSM-Purdue University- Nakshatri/Prasad)

1/1/05 to 12/31/05.

Linking obesity and breast cancer metastasis through CXCR4 and Ship2.

### **COMPLETED IN LAST THREE YEARS**

R21-CA82208, Nakshatri (PI) 5-1-00 to 4-30-02

The Role of IL-1alpha in Metastasis of Breast Cancer

The major goals of the proposal were to determine the role of IL-1alpha in metastasis of breast cancer. The PI is involved in overall supervision, data interpretation and manuscript writing. He was also involved in mammary fat pad injection of nude mice.

00A047, Nakshatri (PI) 7/1/00 to 6/30/03

American Institute for Cancer Research

Feverfew, an Herbal NF- $\kappa$ B Inhibitor, in the Treatment of Breast Cancer

The major goal of this project is to determine whether feverfew inhibits metastasis of breast cancer and increase their response to chemotherapeutic drug taxol. The PI was involved in overall supervision, data interpretation and manuscript writing. He was also involved in mammary fat pad injection of nude mice.

Aventis Pharmaceuticals, Nakshatri (PI) 5/01/02 to 4/30/03

Role of NF- $\kappa$ B Regulated Genes in Resistance to Docetaxel in Breast Cancer

The major goal of this project is to determine whether cIAP-2, Mn-SOD and TRAF-1, three NF- $\kappa$ B regulated genes confer resistance to the chemotherapeutic drug docetaxel. Overlap none. The PI was involved in overall supervision, data interpretation and manuscript writing.

RPG-00-122-01-TBE, Nakshatri (PI) 1/1/2000 to 12/31/2003

American Cancer Society

Effect of ER Phosphorylation on Resistance to TNF and Tamoxifen

The major goals of this project are to identify the amino acids in estrogen receptor that is phosphorylated by tumor necrosis factor induced kinases. Also, we will investigate whether breast cancer cells that are resistant TNF are cross resistant to tamoxifen. The PI was involved in overall supervision, data interpretation and manuscript writing. He was also directly involved in some of the studies.

Principal Investigator/Program Director (Last, First, Middle): Nakshatri, Harikrishna

DAMD17-01-0274 (Nakshatri, H) 08/01/2001 to 07/31/2005

ARMY DOD

NF-KappaB-mediated Repression of GADD153/CHOP: Role in Breast Cancer Initiation

The major goal of this project is determine whether NF- $\kappa$ B promotes transformation of human mammary epithelial cells by repressing the expression of pro-apoptotic, DNA damage inducible gene GADD153/CHOP.

(Nakshatri, H) 05/01/2002 to 04/30/2005

Aventis

Role of NF-kB Regulated Genes in Resistance to Docetaxel in Breast Cancer Cells

The major goal of this project is to determine whether cIAP-2, Mn-SOD and TRAF-1, three NF-kB Regulated Genes Confer Resistance to the Chemotherapeutic Drug Docetaxel

DAMD17-02-1-0072 (Sweeney, C) 04/1/2002 to 03/31/2005

Department of Defense

Targeting Nuclear Factor KappaB for the treatment of Prostate Cancer

The major goal of this project is to determine whether the herb derived NF-kB inhibits the growth and angiogenesis in prostate cancer.

Co-Investigator: H. Nakshatri, PhD

RSG-02-192-01TBE (Nephew, K.) 07/01/2002 to 03/31/2005

American Cancer Society

Regulation of Estrogen Receptor Function by Ubiquitin-like NEDD8 Pathway

This project seeks direct evidence for the involvement of neddylation in the regulation of steroid receptor function and in the growth stimulatory properties of steroids, particularly estrogen, in target cells.

Co-Investigator: H. Nakshatri, PhD

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**BIOGRAPHICAL SKETCH**


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NAME Christie M. Orschell, Ph.D. (published previous to 2002 as Christie M. Traycoff)		POSITION TITLE Associate Scientist/Associate Professor of Medicine	
eRA COMMONS USER NAME corschel			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Indiana University, Indianapolis, IN	B.S.	1986	Medical Technology
Indiana University, Indianapolis, IN	Ph.D.	1992	Pharmacology
Indiana University, Indianapolis, IN	Post-Doc	1992-94	Hematology

**A. Positions and Honors.**

1985-1992 Medical Technologist: Indiana University Hospital and Riley Children's Hospital  
 1987-1992 Graduate Assistant: Dept. of Pharmacology and Toxicology, Indiana University School of Medicine (IUSM)  
 1987-1990 Laboratory Instructor: Medical Pharmacology Laboratory for medical students, IUSM  
 1989-2000 Assistant Instructor: Respiratory Therapy Pharmacology, IUSM  
 1992-1994 Postdoctoral Fellowship: Department of Medicine, Division of Hematology/Oncology, IUSM  
 1994-2001 Director: Molecular Diagnostics Laboratory, Division of Hematology/Oncology, IUSM  
 1994-2000 Assistant Scientist / Assistant Professor of Medicine, Division of Hematology / Oncology, IUSM  
 2000-pres. Associate Scientist / Associate Professor of Medicine, Division of Hematology / Oncology, IUSM

Indiana University Purdue University, Inc. Graduate Fellowship Award; Scholarship: 1987-1988

Indiana University School of Medicine; Fee Scholarship for in-state tuition: 1987-1991

Sigma Xi, Associate member: 1988

American Cancer Society Institutional Grant: 1994-1995

American Society of Clinical Pathologists. Board of Registry, MT (ASCP): 1986

NCCLS Subcommittee on Molecular Genetics: 1995

Gene Therapy and Inborn Errors of Metabolism, NIH Study Section, 2004, 2005

Experimental Hematology, Editorial Board, 2005

**B. Selected peer-reviewed publications (in chronological order).** (Selected from a total of 48)

EF Srour, ED Zanjani, K Cornetta, **CM Traycoff**, AW Flake, M Hedrick, JE Brandt, T Leemhuis, and R Hoffman. Persistence of human multilineage, self-renewing lymphohematopoietic stem cells in chimeric sheep. *Blood*. 82:3333-42, 1993.

**CM Traycoff**, MR Abboud, J Laver, JE Brandt, R Hoffman, P Law, L Ishizawa, and EF Srour. Evaluation of the *in vitro* behavior of phenotypically defined populations of umbilical cord blood hematopoietic progenitor cells. *Exp. Hematol.* 22:215-222, 1994.

**CM Traycoff**, MR Abboud, J Laver, DW Clapp, and EF Srour. Rapid exit from G0/G1 phases of cell cycle in response to stem cell factor confers on umbilical cord blood CD34+ cells an enhanced ex vivo expansion potential. *Exp. Hematol.* 22(13):1264-1272, 1994.

**CM Traycoff**, ST Kosak, S Grigsby, EF Srour. Evaluation of ex vivo expansion potential of CB and BM hematopoietic progenitors using cell tracking and limiting dilution analysis. *Blood* 85(8): 2059-2068, 1995.

**CM Traycoff**, K Cornetta, MC Yoder, A Davidson, EF Srour. Ex vivo expansion of murine hematopoietic progenitor cells generates classes of expanded cells possessing different levels of bone marrow repopulating potential. *Exp. Hematol.* 24(2):299-306, 1996.

**CM Traycoff**, EF Srour, P Dutt, Y Fan, K Cornetta. The 30/35 kDa chymotryptic fragment of fibronectin enhances retroviral-mediated gene transfer in purified chronic myelogenous leukemia bone marrow progenitors. *Leukemia* 11:159-167, January 1997.

K Chen, S Braun, S Lyman, Y Fan, **CM Traycoff**, EA Wiebke, J Gaddy, G Sledge, HE Broxmeyer, K Cornetta. Anti-tumor activity and immunotherapeutic properties of Flt3-ligand in a murine breast cancer model.

Cancer Research 57:3511-3516, August 1997.

**CM Traycoff**, A Orazi, AC Ladd, S Rice, J McMahal, EF Srour. Proliferation-induced decline of primitive hematopoietic progenitor cell activity is coupled with an increase in apoptosis of ex vivo expanded CD34+ cells. *Experimental Hematology* 26(1):53-62, January 1998

**CM Traycoff**, B Halstead, S Rice, J McMahal, EF Srour, and K Cornetta. Chronic myelogenous leukaemia CD34+ cells exit G0/G1 phases of cell cycle more rapidly than normal marrow CD34+ cells. *British Journal of Haematology* 102(3):759-767, August 1998.

Dagher R, Hiatt K, **Traycoff CM**, Srour EF, Yoder MC. c-Kit and CD38 are expressed by reconstituting hematopoietic cells present in murine yolk sac. *Biol. of Blood and Marrow Transplantation* 4:69-74, 1998.

RE Pyatt, LL Jenski, R Allen, K Cornetta, R Abonour, **CM Traycoff**, EF Srour. Use of merocyanine 540 for the isolation of quiescent, primitive human BM hematopoietic progenitor cells. *J Hematother* 8:189-198, 1999.

R Abonour, DA Williams, L Einhorn, KM Hall, J Chen, J Coffman, **CM Traycoff**, A Bank, I Kato, M Ward, SD Williams, R Hromas, MJ Robertson, FO Smith, D Woo, B Mills, EF Srour, and K Cornetta. Efficient retrovirus-mediated transfer of the multidrug resistance 1 gene into autologous human long-term repopulating hematopoietic stem cells. *Nature Medicine* 6(6): 652-658, June 2000.

**CM Orschell-Traycoff**, K Hiatt, RN Dagher, S Rice, MC Yoder, and EF Srour. Homing and engraftment potential of Sca-1+ lin- cells fractionated on the basis of adhesion molecule expression and position in cell cycle. *BLOOD* 96(4):1380-1387, August 2000.

J Wilpshaar, JHF Falkenburg, X Tong, WA Noort, R Breese, DK Heilman, HHH Kanhai, **CM Orschell-Traycoff**, and EF Srour. Similar repopulating capacity of mitotically active and resting umbilical cord blood CD34+ cells in NOD/SCID mice. *BLOOD* 96(6):2100-2107, Sept. 2000.

PA Plett, SM Frankovitz, R Abonour, **CM Orschell-Traycoff**. Proliferation of Human Hematopoietic Bone Marrow Cells in Simulated Microgravity. *In Vitro Cellular & Development Biology-Animal* 37(2):73-78, 2001.

EF Srour, A Jetmore, FM Wolber, PA Plett, R Abonour, MC Yoder, and **CM Orschell-Traycoff**. Homing, cell cycle kinetics and fate of transplanted hematopoietic stem cells. *Leukemia* 15:1681-1684, 2001.

A Jetmore, PA Plett, X Tong, FM Wolber, R Breese, R Abonour, **CM Orschell-Traycoff**, and EF Srour. Homing efficiency, cell cycle kinetics and survival of quiescent and cycling human CD34+ cells transplanted into conditioned NOD/SCID recipients. *BLOOD* 99(5):1585-1593, 2002.

PA Plett, SM Frankovitz, FM Wolber, R Abonour, and **CM Orschell-Traycoff**. Engagement of CXCR4 with SDF-1 $\alpha$  or specific antibody activates circulating CD34+ cells and enhances their NOD/SCID repopulating potential. *Experimental Hematology*, 30:1061-1069, Sept. 2002.

PA Plett, SM Frankovitz, and **CM Orschell-Traycoff**. In vivo trafficking, cell cycle activity, and engraftment potential of phenotypically defined primitive hematopoietic cells after transplantation into irradiated or nonirradiated recipients. *BLOOD* 100(10):3545-3552, Nov. 2002.

J Rehman, J Li, **CM Orschell**, and KL March. Peripheral blood "endothelial progenitor cells" are derived from monocyte-macrophages and secrete angiogenic growth factors. *Circulation* 107:35-40, Feb. 2003.

PA Plett, SM Frankovitz, and **CM Orschell**. Distribution of marrow repopulating cells between bone marrow and spleen early after transplantation. *BLOOD* 102(6):2285-2291, Sept. 2003.

X Li, PA Plett, Y Yang, P Hong, B Freie, EF Srour, **CM Orschell**, DW Clapp, and LS Haneline. Fanconi anemia type C deficient hematopoietic stem/progenitor cells exhibit aberrant cell cycle control. *BLOOD* 102(6):2081-2084, Sept. 2003.

PA Plett, R Abonour, SM Frankovitz, and **CM Orschell**. Impact of modeled microgravity on migration, differentiation, and cell cycle control of primitive human hematopoietic progenitor cells. *Experimental Hematology* 32:773-781, Aug 2004.

BW Freie, SLM Ciccone, X Li, PA Plett, **CM Orschell**, EF Srour, H Hanenberg, D Schindler, S-H Lee, and DW Clapp. A role for the Fanconi anemia C protein in maintaining the DNA damage-induced G2 checkpoint. *JBC*, 279(49):50986-50993, 2004.

EF Srour, X Tong, KW Sung, PA Plett, S Rice, J Daggy, CT Yiannoutsos, R Abonour, **CM Orschell**. Modulation of in vitro proliferation kinetics and primitive hematopoietic potential of individual human CD34+CD38-/lo cells in G0. *Blood*, 105(8):3109-16, April 15, 2005.

Broxmeyer HE, Clapp DW, **Orschell CM**, Hangoc G, Cooper S, Plett PA, Liles WC, Li X, Graham-Evans B, Calandra G, Bridger G, Dale DC, Srour EF. Rapid Mobilization of Murine and Human Hematopoietic Stem and Progenitor Cells with AMD3100, a CXCR4 Antagonist. *J Exp Med*, 201(8):1307-18, 2005.

**C. Research Support:**  
**Ongoing Research Support**

**Source:** NIH/NIAID

**Dates of Project:** 09/30/05-09/30/10

**Title:** Medical Countermeasures Against Radiological Threats: Product Development Support Services.

The goal of this project is to perform hematologic screening and efficacy studies and GLP efficacy studies in irradiated mice for radioprotective drugs in an FDA approved manner.

Role: PI, 25% effort, Indiana University subcontract.

R01 HL75660-01A2

**Dates of Project:** 04/01/05-03/31/09

**Source:** NIH/NHLBI

**Title:** Multifaceted Interventions to Amplify HSC Engraftment

The major goal of this project is to increase the engraftment potential of limited numbers of graft cells through manipulation of the graft, the conditioning regimens of the host, or intrinsic host parameters.

Role: PI, 50% effort

R01 HL75816-01 Kapur (PI)

**Dates of Project:** 01/01/04-12/31/08

**Source:** NIH/NHLBI

**Title:** Mechanisms of Adhesion and Growth Control in Stem Cells

The major goal of this project is to determine how the Src family of signaling molecules regulate growth and actin-based functions in c-Kit+Sca-1+lin- murine cells.

Role: Co-Investigator, 10% effort

Srouf (PI)

**Dates of Project:** fall/05-fall/10

**Source:** NIH/NHLBI

**Title:** Extrinsic Modulation of Hematopoietic Stem Cell Fate

The major goal of this project is to assess the impact of the interaction of stem cells with their hematopoietic microenvironment on stem cell function throughout ontogeny.

Role: Co-Investigator, 15% effort

U24 RR11148 Cornetta (PI)

**Dates of Project:** 8/1/95 - 8/31/07

**Source:** NIH/NIRR

**Title:** National Gene Vector Laboratory

The major goal of this project is to produce clinical grade vector supernatant for investigators world-wide under GMP and GLP regulations.

Role: Co-Investigator, 10% effort

C-111 Srouf (PI)

**Dates of Project:** 07/22/02 – 06/19/05

**Source:** Anormed, Inc.

**Title:** Analysis of the Effect of AMD-3100 When Given Alone or With G-CSF to Mobilize Progenitor Cells After Pre-Treatment with G-CSF.

The major goal of this study is to characterize the functional capacity of human CD34+ cells mobilized by the CXCR4 antagonist, AMD-3100, alone or in concert with G-CSF.

Role: Co-Investigator

Orschell, Cripe, Chan (co-PIs)

**Dates of Project:** 10/01/03 - 09/30/05

**Source:** Indiana University Cancer Center. Hematopoiesis and Immunology Program

**Title:** Epigenetic Changes in Myelodysplastic Syndromes

The major goal of this project is to examine epigenetic alterations in erythropoiesis in myelodysplasia

Role: co-PI

Orschell (PI)

**Dates of Project:** 09/01/04 - 08/31/05

**Source:** IUSM Biomedical Research Group

**Title:** Enhanced Hematopoietic Stem Cell Engraftment Through the Use of SDF-1.

The major goal of this project is to understand how treatment of graft cells with SDF-1 prior to transplantation increases their engraftment potential.

Role: PI

### **Completed Research Support:**

Orschell (PI)

**Dates of Project:** 01/01/02 – 12/31/02

**Source:** Indiana University Core Centers of Excellence in Molecular Hematology

**Title:** Temporal Effects of Radiation Dosing on Success of Bone Marrow Transplantation.

The major goal of this project is to investigate how timing of irradiation and transplantation affect homing and engraftment potential of transplanted stem cells.

Role: PI

Orschell (PI)

**Dates of Project:** 01/01/01 - 12/31/01

**Source:** Indiana University Core Centers of Excellence in Molecular Hematology

**Title:** Bi-functional concentration-dependent mechanisms elicit different CXCR4 responses in primitive hematopoietic progenitor cells.

The major goal of this project is to investigate the dose-related mechanisms CXCR4 ligands on the in vivo function of primitive hematopoietic progenitor cells.

Role: PI

PHS R01 HL55716-05 Srour (PI)

**Dates of Project:** 07/01/00 – 06/30/04

**Source:** NIH

**Title:** Cell Cycle Progression and Hematopoietic Potential

The major goal of this project is to examine the functional similarities and differences between different sources of hematopoietic progenitor cells and the suitability of each source for stem cell transplantation.

Role: Co-Investigator

PHS R01 HL62200 Srour (PI)

**Dates of Project:** 04/01/99 - 03/31/03

**Source:** NIH

**Title:** Adhesion Analysis of Cycling Stem Cells Through Ontogeny

The major goal of this project is to better understand the mechanisms of homing of HSC during mammalian embryonic development and postnatal trafficking of these cells.

Role: Co-Investigator

NAG-1586 Orschell (PI)

**Dates of Project:** 01/01/99 - 12/31/02

**Source:** NASA

**Title:** Self Renewal Replication of Hematopoietic Stem Cells in Microgravity

The major goal of this study is to investigate, using the RWV bioreactor, how ex vivo culture under simulated microgravity conditions, coupled with a more architecturally "correct" BM microenvironment, affect cell cycle activation and proliferation of highly purified populations of primitive HPC.

Role: PI

U24 RR11148 Cornetta (PI)

**Dates of Project:** 09/01/96 – 08/31/04

**Source:** NIH/NIRR

**Title:** National Gene Vector Lab

The major goal of this study is to develop a national gene vector laboratory for the production of clinical grade gene vectors.

Role: Co-Investigator

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Louis M. Pelus, Ph.D.	POSITION TITLE Professor		
eRA COMMONS USER NAME lpelus	Dept Microbiology and Immunology Associate Director, Walther Oncology Center		
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Queens College, CUNY, New York	B.A.	1973	Biology
Rutgers University, New Jersey	M.S.	1977	Zoology
Rutgers University, New Jersey	Ph.D.	1977	Immunology
Sloan Kettering Institute, New York	Postdoc	1977-1978	Cell Biology
Sloan Kettering Institute, New York	Postdoc	1978-1980	Exp Hematology

**A. Positions and Honors.**

09/73 - 01/77	Graduate Teaching Fellowship, Department of Zoology, Rutgers University, New Jersey.
01/76 - 01/77	Research Fellow, Merck Institute for Therapeutic Research, Department of Inflammation, Merck Research Laboratories, New Jersey
01/77 - 01/78	Associate Researcher (NIH Postdoctoral Fellow), Department of Calcium Metabolism, Sloan Kettering Institute, New York; <u>NRSA Award, NCI</u>
02/78 - 02/80	Associate Researcher (NIH Postdoctoral Fellow), Department of Developmental Hematopoiesis, Sloan Kettering Institute, New York; <u>NRSA Award, NCI</u>
01/80 - 09/82	Research Associate, Department of Developmental Hematopoiesis, Sloan Kettering Institute, New York; <u>Special Fellowship, Leukemia Society of America; Young Investigator Award, NCI.</u>
09/82 - 10/86	Assistant Member, Department of Developmental Hematopoiesis, Sloan Kettering Institute, New York; <u>Scholar Award, Leukemia Society of America.</u> Assistant Professor, Sloan Kettering Division-Graduate School of Medical Sciences, Cornell University, New York.
06/86 - 10/89	Assistant Member and Head, Department of Hematopoietic Regulation, Sloan Kettering Institute, N.Y. Assistant Professor, Sloan Kettering Division-Graduate School of Medical Sciences, Cornell University, New York.
10/89 - 01/90	Senior Scientist, Department of Immunology, SmithKline Beecham Pharmaceuticals, Pennsylvania
01/90 - 10/91	Senior Scientist, Department of Anti-Infectives, SmithKline Beecham Pharmaceuticals, Pennsylvania
10/91 - 06/95	Assistant Director, Department of Anti-Infectives, SmithKline Beecham Pharmaceuticals, Pennsylvania
05/92 - 06/95	Assistant Director, Department of Molecular Virology and Host Defense, SmithKline Beecham Pharmaceuticals, Pennsylvania
06/95 - 11/98	Associate Director, Department of Molecular Virology and Host Defense, SmithKline Beecham Pharmaceuticals, Pennsylvania
05/99 - 07/04	Associate Scientist, Associate Professor-part time, Department of Microbiology and Immunology, Associate Director, Walther Oncology Center, Indiana University School of Medicine, IN.
08/04 - present	Professor, Department of Microbiology and Immunology, Associate Director, Walther Oncology Center, Indiana University School of Medicine, IN.

**Memberships:**

Review Committees: Past. NCI Site Visit 1986-1988. Ad Hoc Reviewer: NCI, NHLB, NIAID, 1986-1988.

Review Committees: Present. Ad Hoc Hematology 2, 3/02; NHLBI 7/02; NCI Program Project Review 10/02; Ad Hoc Reviewer Hem 1, 2/03, NHLBI RFA 3/03

Member, Hematopoiesis Study Section, October 2004-July 2008  
Societies: ASH, ISEH, AAI, ASM, AACR, AAAS, ISHAGE, NYAS

## B. Selected peer-reviewed publications (from 104)

D Lovhaug, LM Pelus, EM Nordie, A Boyum, MAS Moore. Monocyte conditioned medium induces GM-CSF production in the adherent cell layer of murine bone marrow cultures. *Exp Hematol* 14:1037-1042, 1986.

P Gentile, LM Pelus. In vivo modulation of Myelopoiesis by prostaglandin E. II. Inhibition of granulocyte-monocyte progenitor cell (CFU-GM) cell cycle rate. *Exp Hematol* 15:119-126, 1987.

L Lu, LM Pelus, W Piacibello, MAS Moore, W Hu, HE Broxmeyer. Prostaglandin E acts at two levels to enhance colony formation in vitro by erythroid (BFU-E) progenitor cells. *Exp Hematol* 15:765-771, 1987.

S Leitner, LM Pelus, C Cappello, G Bosl. Abnormal colony formation and prostaglandin E responsiveness of myeloid progenitor cells in patients cured of germ cell neoplasms after combination chemotherapy. *Cancer* 60:312-317, 1987.

NA Kernan, NH Collins, I Cunningham, H Castro-Malaspina, N Flomenberg, S Gulati, J Brochstein, D Emanuel, J Laver, C Keever, C Bordignon, J Burns, J Frame, T Small, A Gillio, MA Bonilla, A Pecora, B Kushner, C Quijana, LM Pelus, K Welte, RJ O'Reilly. Prevention of GVHD in HLA-Identical marrow grafts by removal of T cells with soybean agglutinin and SRBCA. *Bone Marrow Transplant* 2:13-18, 1987.

LM Pelus, O Ottmann, K Nocka. Synergistic inhibition of human marrow granulocyte-macrophage progenitor cells by prostaglandin E and recombinant interferons alpha, beta and gamma. An effect mediated by tumor necrosis factor. *J Immunol* 140:479-484, 1988.

LM Pelus, P Gentile. In vivo modulation of myelopoiesis by prostaglandin E2. III. Induction of suppressor cells in marrow and spleen capable of mediating inhibition of CFU-GM proliferation. *Blood* 71:1633-1640, 1988.

LM Pelus, S Vadhan-Raj. Modulation of responsiveness of chronic myelogenous leukemia granulocyte-macrophage colony-forming cells to growth regulation following in vivo treatment with recombinant  $\gamma$ -interferon. *Am J Hematol* 28:21-26, 1988.

KH Nocka, LM Pelus. Cell cycle effects of deferoxamine on human and murine hematopoietic progenitor cells. *Cancer Res* 48:3571-3575, 1988.

OG Ottmann, LM Pelus. Differential proliferative effects of transforming growth factor- $\beta$  on human hematopoietic progenitor cells. *J Immunol* 140:2661-2665, 1988.

PS Gentile, LM Pelus. In vivo modulation of myelopoiesis by prostaglandin E2. IV. Prostaglandin E2 induction of myelopoietic inhibitory activity. *J Immunol* 141:2714-2720, 1988.

OG Ottmann, KH Nocka, MAS Moore, LM Pelus. Differential expression of class II MHC antigens in subpopulations of human hematopoietic progenitor cells. *Leukemia* 2:677-686, 1988

LM Pelus, E Levi, K Welte. The response of human marrow colony-forming units granulocyte-macrophage to inhibition by prostaglandin E and acidic isoferitins is associated with expression of MHC class II antigens and requires the participation of a CD8+ T lymphokine. *J Immunol* 141:1658-1664, 1988.

OG Ottmann, M Abboud, K Welte, LM Souza, LM Pelus. Stimulation of human hematopoietic progenitor cell proliferation and differentiation by recombinant human Interleukin 3. Comparison and interactions with recombinant human granulocyte-macrophage and granulocyte colony-stimulating factors. *Exp Hematol* 17:191-197, 1989.

LM Pelus. Modulation of myelopoiesis by prostaglandin E2: Demonstration of a novel mechanism of action in vivo. *Immunol Res* 8:176-184, 1989.

LM Pelus. Blockade of prostaglandin biosynthesis in intact mice dramatically augments the expansion of committed myeloid progenitor cells (colony-forming units-granulocyte, macrophage) after acute administration of recombinant human IL1 $\alpha$ . *J Immunol* 143:4171-4179, 1989.

KH Nocka, OG Ottmann, LM Pelus. The role of marrow accessory cell populations in the augmentation of human erythroid progenitor cell (BFU-E) proliferation by prostaglandin E. *Leukemia Res* 13:527-534, 1989.

JE Talmadge, PL Black, LM Pelus, F Abe. Hematopoietic and hematologic properties of bestatin in normal and cyclophosphamide myelosuppressed mice. *Biomed Pharmacother* 45:61-69, 1991.

AG King, JE Talmadge, AM Badger and LM Pelus. Regulation of colony stimulating activity production from bone marrow cells by the hemoregulatory peptide HP-5. *Exp Hematol* 20:223-228, 1992.

LM Pelus, AG King, HE Broxmeyer, PL DeMarsh, SR Petteway, PK Bhatnagar. Modulation of murine hematopoiesis in vivo by a novel hemoregulatory peptide. *Exp Hematol* 22:239-247, 1994.

PL DeMarsh, SK Succolowski, CL Frey, PK Bhatnagar, Y Koltin, P Actor, LM Pelus, SR Petteway. The hemoregulatory peptide, SK&F 107647, in combination with antifungal therapy in murine *Candida albicans* infections. *Can J Botany*, 73: 1199-1205, 1995.

DP Brooks, LC Contino, S Perez and LM Pelus. Responsiveness of rats with chronic renal failure-induced anemia to recombinant human erythropoietin. *Pharmacology Communications* 6: 319-325, 1995.

PK Bhatnagar, EK Agner, D Alberts, BE Arbo, JF Callahan, AS Cuthbertson, SJ Engelsen, H Fjerdningstad, M Hartmann, D Heerding, J Hiebl, WF Huffman, M Hysben, AG King, P Kremminger, C Kwon, S LoCastro, D Løvhaug, LM Pelus, S Petteway, and JS Takata. Structure-activity relationships of novel hematoregulatory peptides. *J Med Chem*, 39: 3814-3819, 1996.

PK Bhatnagar, D Alberts, JF Callahan, D Heerding, WF Huffman, AG King, S LoCastro, JS Takata and LM Pelus. Development of a pharmacophore model for a novel hematoregulatory peptide. *J Am Chem Soc*, 118: 12862-12863, 1996.

CH Kim, LM Pelus, JR White, E Applebaum, K Johanson, and HE Broxmeyer. CK $\beta$ 11/Macrophage inflammatory Protein-3 $\beta$ /EBI1-Ligand Chemokine is an efficacious chemoattractant for T and B cells. *J Immunol* 160: 2418-2424, 1998.

CH Kim, LM Pelus, JR White, and HE Broxmeyer. Differential chemotactic behavior of developing T cells in response to thymic chemokines. *Blood* 91: 4434-4443, 1998.

SS Tian, P Lamb, AG King, S Miller, L Kessler, JI Luengo, L Averill, RK Johnson, JG Gleason, LM Pelus, SB Dillon, J Rosen. A small, non-peptidyl mimic of Granulocyte-Colony stimulating factor. *Science* 281: 257-259, 1998.

CH Kim, LM Pelus, JR White, and HE Broxmeyer. CK $\beta$ 11/MIP-3 $\beta$ /ELC, a CC chemokine, is a chemoattractant with a specificity for macrophage progenitors amongst myeloid progenitors. *J Immunol*, 161: 2580-2585, 1998.

HE Broxmeyer, CH Kim, SH Cooper, G Hangoc, R Hromas, and LM Pelus. Effects of CC, CXC, C and CX3C chemokines on proliferation of myeloid progenitor cells, and insights into SDF-1 induced chemotaxis of progenitors. *Anal NY Acad Sci*, 872: 142-163, 1999.

CH Kim, LM Pelus, E Appelbaum, K Johanson, N Anzai, HE Broxmeyer. CCR7 ligands, SLC6CKine/Exodus 2 and CK $\beta$ 11/MIP3 $\beta$ /ELC, are chemoattractants for CD56+CD16- NK cells and late stage lymphoid progenitors. *Cell Immunol*, 193: 226-235, 1999.

AG King, K Johanson, CL Frey, PL DeMarsh, P McDevitt, D McNulty, J Balcarek, ZL Jonak, PK Bhatnagar, and LM Pelus. Identification of unique truncated KC/GRO $\beta$  chemokines with potent hematopoietic and anti-infective activities. *J Immunol*, 164: 3774-3782, 2000.

DW Wu, SB Dillon, D Dunnington, T Yi, C Jones, LM Pelus. Hematopoietic cell phosphatase association with JAK2 Kinase in UT7/Epo cells. *Blood Cells, Molecules & Dis* 26:15-24, 2000.

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S Fukuda, DW Wu, K Stark, LM Pelus. Cloning and characterization of a proliferation-associated cytokine-inducible protein, CIP29. *Biochem Biophys Res Comm* 292: 593-600, 2002.

S Fukuda, RG Foster, SB Porter, LM Pelus. The antiapoptosis protein survivin is associated with cell cycle entry of normal cord blood CD34<sup>+</sup> cells and modulates cell cycle and proliferation of mouse hematopoietic cells. *Blood* 100: 2463-2471, 2002.

LM Pelus, D Horowitz, SC Cooper, AG King. Peripheral blood stem cell mobilization. A role for CXC chemokines. *Crit Rev Oncol/Hematol* 43:257-275, 2002.

S Fukuda and LM Pelus. Elevation of Survivin levels by hematopoietic growth factors occurs in quiescent CD34<sup>+</sup> hematopoietic stem and progenitor cells before cell cycle entry. *Cell Cycle* 1: 322-326, 2003.

S Fukuda, CR Mantel and LM Pelus. Survivin Regulates Hematopoietic Progenitor Cell Proliferation through p21<sup>WAF1/Cip1</sup> Dependent and Independent Pathways. *Blood* 103: 120-127, 2004.

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A Merzouk, D Wong, H Salari, H Bian, S Fukuda and LM Pelus. Rational design of chemokine SDF-1 analogs with agonist activity for the CXCR4 receptor and the capacity to rapidly mobilize PMN and hematopoietic progenitor cells in mice. *Letters in Drug Design and Discovery* 1:126-134, 2004.

LM Pelus and S Fukuda. Survivin regulates cell-cycle, survival and proliferation of cord blood CD34+ cells. *In Cord Blood: Biology, Immunology, Banking and Clinical Transplantation*. Ed. H Broxmeyer, AABB Press, Rockville, MD, pages 23-46.

Z Wang, S Fukuda and LM Pelus. Survivin regulates the p53 tumor suppressor gene family. *Oncogene* 23:8146-8153, 2004.

S Fukuda and LM Pelus. Growth factor independent survival and proliferation in hematopoietic cells mediated by activated H-Ras requires the inhibitor of apoptosis protein Survivin. *BBRC* 323:636-644, 2004.

S Okabe, S Fukuda, Y-J Kim, M Niki, LM Pelus, K Ohyashiki, PP Pandolfi, HE Broxmeyer. Stromal Cell-derived factor-1 $\alpha$ /CXCL12-induced chemotaxis of T cells involves activation of the RasGAP-associated docking protein p62Dok-1. *Blood* 105: 474-480, 2005.

S Fukuda, HE Broxmeyer and LM Pelus. Flt3-ligand and Flt3 regulate hematopoietic cell migration by modulating the SDF-1 $\alpha$ (CXCL12)/CXCR4 axis. *Blood* 105:3117-3126, 2005.

LM Pelus, H Bian, S Fukuda, D Wong, A Merzouk, H Salari. CTCE-0021, a peptide agonist of stromal cell-derived factor-1 $\alpha$  (SDF-1 $\alpha$ )/CXCL12 rapidly mobilizes polymorphonuclear neutrophils and hematopoietic progenitor cells into peripheral blood and synergizes with G-CSF. *Exp. Hematol*, 33:295-307, 2005.

C Mantel, Y Guo, H Shibayama, S Fukuda, C Kauffman, LM Pelus, YC Yoder, HE Broxmeyer. Cell cycle checkpoint adaption and apoptosis are uncoupled in mouse ES cell lines. *Blood*, in revision.

Z Wang, S Fukuda, LM Pelus. Disruption of the inhibitor of apoptosis protein, Survivin, sensitizes Bcr-abl positive cells to STI571-induced apoptosis. *Cancer Res* 68:8224-8232, 2005.

S Fukuda, H Bian, AG King, LM Pelus. Rapid engraftment following transplantation with hematopoietic stem and progenitor cells mobilized by the CXC chemokine GRO $\beta$ T (CXCL2 $_{\Delta 4}$ ) is associated with enhanced homing to recipient bone marrow that is not coupled with the SDF-1 $\alpha$  (CXCL12):CXCR4 axis. *Blood*, submitted.

LM Pelus, H Bian, AG King, S Fukuda. Peripheral Blood Stem Cell Mobilization by the CXCR2 chemokine GRO $\beta$ -T/CXCL2 $_{\Delta 4}$  Results from Alteration in the Stoichiometry and Kinetics between Neutrophil-derived pro-Matrix Metalloproteinase-9 (proMMP-9) and the tissue Inhibitor of Metalloproteinase-1 (TIMP-1). *JEM*, submitted.

### C. Research Support.

#### Ongoing Research Support

1 R01 HL 69669-01 Pelus (PI) 8/15/01 – 7/31/06 50%  
NIH/NHLBI Direct: \$225,000/yr Total Direct: \$900,000  
Chemokine induced hematopoietic stem cell mobilization

The major goals of this project are to define the characteristics of chemokine mobilized hematopoietic stem cells mobilized by the CXC chemokines GRO $\beta$  and GRO $\beta$ -T and the mechanisms responsible for chemokine induced hematopoietic stem cell mobilization.

Role: PI

1 R01 HL 079654-01 Pelus (PI) 7/1/04 – 6/30/08 30%  
NIH/NHLBI Direct: \$225,000/yr Total Direct: \$900,000

Role of Survivin in blood stem cell cycle and apoptosis

The major goals of this project are to define the hematopoietic functions of Survivin in regulation of cell cycle and interactions with the p53 family of tumor suppressors.

Role: PI

#### Past

R01 CA33225-12 Pelus (PI) NCI 1982-1993

Regulation of myeloid progenitor cell differentiation

This grant was renewed 3 times and ran 12 years. The grant was transferred to SmithKline Beecham with the PI and voluntarily not renewed due to SmithKline Beecham workload.

Role: PI

R23 CA28512 Pelus (PI) NCI 1980-1982

Regulation of normal and leukemic myeloid stem cells

Role: PI

Principal Investigator/Program Director (Last, First, Middle): **PI Name**

F32 CA05904 Pelus (PI) NCI 1977-1980

Regulation of calcium metabolism and immunosuppression by tumor derived prostaglandin E

Role: PI

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed for Form Page 2.

Follow the sample format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME <b>Karen E. Pollok, Ph.D.</b>		POSITION TITLE <b>Research Assistant Professor</b>	
EDUCATION/TRAINING ( <i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i> )			
INSTITUTION AND LOCATION	DEGREE ( <i>if applicable</i> )	YEAR(s)	FIELD OF STUDY
College of William and Mary, Williamsburg, VA.	B.S.	1979-1983	Biology
University of Kentucky, Lexington, KY.	Ph.D.	1985-1990	Immunology
Microbiology & Immunology, Indiana University, Indianapolis, IN.		1990-1994	Postdoc-Immunology Mentor-Byoung S. Kwon, PhD
Herman B Wells Center for Pediatric Research, Indiana University, Indianapolis, IN.		1994-1997	Sr. Postdoc-Hematology Mentor-David Emanuel, MD

**PROFESSIONAL EXPERIENCE:**

1983-1985 Technical Coordinator, Old Dominion Eye Bank, Alexandria, VA.  
 1997-2000 Assistant Scientist; mentor-David A. Williams, M.D., Herman B Wells Center for Pediatric Research.  
 2000-2005 Assistant Research Professor. Herman B Wells Center for Pediatric Research.  
 2005- Assistant Professor. Pediatric Hematology/Oncology; Herman B Wells Center for Pediatric Research.

**HONORS AND AWARDS:**

1985-1990 Lucille P. Markey Predoctoral Fellowship  
 1989 1<sup>st</sup> Place in the Graduate Research Competition-1989 Mid-West Autumn Immunology Conference, St. Louis, MO.  
 1992 2<sup>nd</sup> Place in the Fellow Research Competition-1992 Mid-West Autumn Immunology Conference, Chicago, IL  
 1993-1994 National Research Service Award (NRSA) fellowship, NIH.  
 1995-1996 American Cancer Society Institutional junior investigator grant

**SELECTED PEER REVIEWED PUBLICATIONS (out of 34):**

1. S. Cai, J.R. Hartwell, R.J. Cooper, B.E. Juliar, E. Kreklau, R. Abonour, W.S. Goebel, and K.E. Pollok. In vivo effects of myeloablative alkylator therapy on survival and differentiation of MGMT<sup>P140K</sup>-transduced human G-CSF-mobilized peripheral blood cells. *Submitted*.
2. S. Cai, Y. Xu, R.J. Cooper, M.J. Ferkowicz, J.R. Hartwell, K.E. Pollok, and M.R. Kelley. Mitochondrial targeting of human O<sup>6</sup>-methylguanine DNA methyltransferase protects against cell killing by chemotherapeutic alkylating agents. 2005. *Cancer Research*. 65: 3319-3327.
3. A.Villella, J. Yao, R. Getty, B. Juliar, C. Yiannoutsos, K. Cornetta, D. Williams and K.E. Pollok. Real-time PCR: an effective tool for measuring transduction efficiency in human hematopoietic progenitor cells. 2005. *Molecular Therapy*. 11:483-491.
4. C.A. Kahl, K. Pollok, L.S. Haneline, and K. Cornetta. Lentiviral Vectors Pseudotyped with Glycoproteins from Ross River and Vesicular Stomatitis Viruses: Variable Transduction Related to Cell Type and Culture Conditions. 2005. *Molecular Therapy*. 11:470-481.
5. D.A. Ingram, L.E. Mead, H.Tanaka, V. Mead, A.Fenoglio, K.Mortell, K.E.Pollok, M.J. Ferkowicz, D. Gilley, and M.C. Yoder. Identification of a novel hierarchy of endothelial progenitor cells utilizing human peripheral and umbilical cord blood. 2004. *Blood*. 104:2752-2760.
6. L. Sastry, Y. Xu, R. Cooper, K. Pollok, and K. Cornetta. Evaluation of plasmid DNA removal from lentiviral vectors by benzonase treatment. 2004. *Human Gene Therapy*. 221-226.
7. E. L. Kreklau, K.E. Pollok, J.R. Hartwell, R.J. Cooper, D.A. Williams, and L.C. Erickson. 2003. Hematopoietic expression of O<sup>6</sup>-methylguanine DNA methyl-transferase-P140K allows intensive treatment of human glioma xenografts with combination O<sup>6</sup>-benzylguanine and 1,3-bis-(2-chloroethyl)-1-nitrosourea. *Molecular Cancer Therapeutics*. 2: 1321-1329.
8. K.E. Pollok, J.R. Hartwell, A. Braber, R.J. Cooper, M. Jansen, S. Ragg, B.J. Bailey, L.C. Erickson, E.L. Kreklau, and D.A. Williams. Effective *in vivo* selection of human hematopoietic cells in a xenograft model using combined pharmacologic and genetic manipulations. 2003. *Human Gene Therapy* 14:1703-1714.
9. E.J. Woods, J. Liu, K.E. Pollok, J.R. Hartwell, F.O. Smith, D.A. Williams, M.C. Yoder, and J.K. Critser. 2003. A theoretically optimized method for cord blood stem cell cryopreservation. *Journal of Hematotherapy and Stem Cell Research*. 12:341-350.

10. C.Leurs, M. Jansen, K.E. Pollok, M. Heinkelein, M. Schmidt, M. Wissler, D. Lindemann, C. Von Kalle, A., Rethwilm, D.A. Williams, and H. Hanenberg, H. 2003. Comparison of three retroviral vector systems for the transduction of NOD/SCID repopulating CD34<sup>+</sup> CB cells. *Human Gene Therapy* 14: 509-519.
11. H. Hanenberg, S.D. Batish, K.E. Pollok, L. Vieten, P.C. Verlander, C. Leurs, R.J. Cooper, K. Gottsche, L. Haneline, D.W. Clapp, S. Lobitz, D.A. Williams, A.D. Auerbach. 2002. Phenotypic correction of primary Fanconi anemia T cell with retroviral vectors as a diagnostic tool. *Experimental Hematology* 30: 410-420.
12. K.E. Pollok, J.C.M. van der Loo, R.J. Cooper, J.R. Hartwell, K.R. Miles and D.A. Williams. 2001. Differential Transduction Efficiency of SCID-repopulating cells derived from umbilical cord blood and G-CSF-mobilized peripheral blood. *Human Gene Therapy* 12: 2099-2112.
13. Q. Sun, K.E. Pollok, R.L. Burton, L.J. Dai, W. Britt, D.J. Emanuel, and K.G. Lucas. 1999. Simultaneous *ex vivo* expansion of cytomegalovirus and Epstein-Barr virus specific cytotoxic T-lymphocytes using B-lymphoblastoid cell lines expressing CMV pp65. *Blood* 94: 3242-3250.
14. Q. Sun, R.L. Burton, K.E. Pollok, D.J. Emanuel, and K.G. Lucas. 1999. CD4<sup>+</sup> Epstein-Barr virus specific cytotoxic T-lymphocytes from umbilical cord blood. *Cellular Immunology* 195: 81-88.
15. K.E. Pollok, J.C.M. van der Loo, R.J. Cooper, L. Kennedy, and D.A. Williams. 1999. Costimulation of transduced T lymphocytes via T-cell receptor/CD3 complex and CD28 leads to increased transcription of integrated retrovirus. *Human Gene Therapy* 10: 2221-2236.
16. E. MacNeill, H. Hanenberg, K.E. Pollok, J.C.M. van der Loo, M.F.A. Bierhuizen, G. Wagemaker, and D.A. Williams. 1999. Simultaneous infection with retroviruses pseudotyped with different envelope proteins bypasses viral receptor gp70 and target cells on fibronectin CH-296. *Journal of Virology* 73: 3960-3967.
17. V. Dardahlon, N. Noraz, K. Pollok, C. Rebouissou, M. Boyer, A.Q. Bakker, H. Spits, and N. Taylor. 1999. Green fluorescent protein as a selectable marker of fibronectin-facilitated retroviral gene transfer in primary human T lymphocytes. *Human Gene Therapy* 10: 5-14.
18. K.E. Pollok, H. Hanenberg, T.W. Noblitt, W.L. Schroeder, I. Kato, D.Emanuel, and D.A. Williams. 1998. High-efficiency gene transfer into normal and adenosine deaminase-deficient T-lymphocytes is mediated by transduction on recombinant fibronectin fragments. *Journal of Virology*. 72: 4882-4892.
19. K.G. Lucas, R.L. Burton, D.K. Heilman, K.E. Pollok, D. Emanuel. 1997. Cord blood mononuclear cell transformation assay for screening for the presence of Epstein-Barr virus. *Journal of Hematotherapy* 6: 587-590.
20. J.C. Hurtado, S.H. Kim, K.E. Pollok, Z.H. Lee, and B.S. Kwon. 1995. Potential role of 4-1BB in T cell activation-comparison with the costimulatory molecule CD28. *Journal of Immunology* 155: 3360-3367.
21. K.E. Pollok, S.H. Kim, and B.S. Kwon. 1995. Regulation of 4-1BB expression by cell-cell interactions and the cytokines, interleukin-2 and interleukin-4. *European Journal of Immunology* 25: 488-494.
22. K.E. Pollok, Y-J. Kim, J. Hurtado, Z. Zhou, and B.S. Kwon. 1994. 4-1BB T cell antigen binds to mature B cells and macrophages, and costimulates anti- $\mu$ -primed splenic B cells. *European Journal of Immunology*. 24: 367-374.
23. K.E. Pollok, Y-J. Kim, Z. Zhou, J. Hurtado, K.K. Kim, R.T. Pickard and B.S. Kwon. 1993. Inducible T cell antigen 4-1BB: analysis of expression and function. *Journal of Immunology* 150: 771-781.
24. K.E. Pollok, V. O'Brien, L. Marshall, J.W. Olson, R.J. Noelle, and E.C. Snow. 1991. The Development of Competence in Resting B Cells: the induction of cAMP and ornithine decarboxylase activity following direct contact between B and Helper T cells. *Journal of Immunology* 146: 1633-1641.

#### **SELECTED BOOK CHAPTERS AND REVIEWS (out of 6):**

1. K.E. Pollok. *In vivo* protection of hematopoietic cells from alkylator-mediated DNA damage. 2003. *Current Hematology Reports*. 2:341-347.
2. D.A. Williams, E. MacNeill, H. Hanenberg, H. van der Loo, and K.Pollok. 2000. *In "Transplantation in Hematology and Oncology"* (T. Büchner, H. Jürgens, W. E. Berdel, J. van de Loo, J. Ritter, J. Kienast, and J. Vormoor, eds.), pp. 333-336. Springer, Berlin Heidelberg.

#### **SELECTED ABSTRACTS (out of 41):**

1. S. Zhang, K. Pollok, L. Sastry, L. Berthoux, J. Luban, and K. Cornetta. 2005. Cellular Mechanisms involved with lentiviral gene transfer. Oral Presentation. American Society for Gene Therapy. *Molecular Therapy* 11: S1.
2. S. Cai, J.R. Hartwell, A.G. Ernstberger, W.S. Goebel, H. Hanenberg, and K.E. Pollok. 2005. Transduction of minimally stimulated hematopoietic progenitor cells with a foamy virus vector that expresses MGMTP140K. American Society for Gene Therapy. *Molecular Therapy* 11: S184.
3. S. Cai, J.R. Hartwell, R. J. Cooper, and K.E. Pollok. Analysis of secondary reconstitution in NOD/SCID mice utilizing *in vivo*-selected O<sup>6</sup>-methylguanine DNA methyltransferase P140K (MGMT<sup>P140K</sup>)-transduced umbilical cord blood. 2004. *Oral presentation, Presidential Symposium*. International Society for Experimental Hematology.

**OTHER SUPPORT:**

ACTIVE FUNDING:

**Source: Hope Street Kids Foundation**

Role: Principal Investigator

Title: "*Protection of hematopoietic stem and progenitor cells in a pediatric brain tumor xenograft model*"

Dates of proposed project: 7/1/04 – 6/30/06

Major goals of the project: development of a model to study the effect of high-dose alkylator therapy on hematopoietic stem-cell function and glioma cell growth.

**Source: Collaboration in Biomedical Research Award**

Role: Principal Investigator

Title: "*Monitoring Cell Trafficking In Vivo Using Non-invasive Biomedical Imaging Techniques*"

Dates of proposed project: 1/1/05 – 12/31/05

Major goals of the project: development and validate noninvasive imaging technology for cell trafficking studies

**Source: NIH/NIDDK**

Grant number: P30 DK49218

Role: Co-Principal investigator, Mouse Core; PI: Srour

Title: "Core Centers of Excellence in Molecular Hematology"

Dates of proposed project: 9/1/99 – 8/31/05

Major goals of the project: supervise and maintain NOD/SCID breeding colony for investigators

**Source: NIH**

Role: Co-Principal Investigator

Title: "*Imbalancing DNA BER to enhance ovarian tumor sensitivity*"

Dates of proposed project: 4/1/04 – 3/31/09

Annual Direct Cost/Percent effort: \$250,000 / 15%

Major goals: Knocking down or inhibiting the human AP endonuclease APE1 or overexpressing MPG to sensitize tumor cells to chemo or IR.

**Source: NIH**

Grant number: U24 RR011148

Role: Co-investigator

Title: "National Gene Vector Laboratory at Indiana University"

Dates of proposed project: 9/1/03 – 8/31/05

Major goals of the project: generation of retrovirus supernatants for clinical gene therapy trials.

**Pending Funding:**

**Source: NIH**

Role: Principal Investigator

Title: "*Mitochondrial genome protection in hematopoietic stem cells*"

Dates of proposed project: 12/31/05 – 12/30/10

Annual Direct Cost/Percent effort: \$250,000 / 50%

Major goals of the project: gain an understanding of hematopoietic stem-cell behavior during alkylator therapy and to develop optimal modes of DNA repair that protect these cells from alkylator-mediated DNA damage.

PREVIOUS FUNDING (past 3 years):

- SBIR/NIH (R44 HL065864), Co-investigator; Principal Investigator-Erik Woods, Ph.D., "A novel frozen storage system for cord blood stem cells." 2/12/03-1/31/05.
- Eli Lilly and Company, Contract, Principal Investigator, "In vivo tumor modeling for lymphoma and glioma." 10/1/03-3/31/05

- Biomedical Research Grant by IU School of Medicine, Principal Investigator, “Alkylator-resistant Hematopoietic stem cells,” 11/-1/04-10/31/04.
- Pilot Project funded by IU Radiology Department (NIH/NCI), Principal Investigator, “*In vivo PET imaging analysis of chemotherapy-resistant human hematopoietic stem cells in a lymphoma-xenograft model,*” 3/1/02 – 4/30/04.
- Pilot Project Funded by IU Cancer Center (NIH), Principal Investigator, “*Chemoprotection of human stem and progenitor cells in lymphoma–xenograft model by repair of alkylator-induced mitochondrial and nuclear DNA damage,*” 4/26/02 – 4/30/04.
- IU Core Centers of Excellence in Molecular Hematology (NIH), Principal Investigator, “Analysis of chemotherapy-resistant human hematopoietic stem and progenitor cells in a lymphoma-xenograft model,” 1/1/01 – 12/31/03
- Showalter Research Trust Fund, Principal Investigator, “*In vivo analysis of chemotherapy-resistant human hematopoietic stem and progenitor cells;*” 7/01/01-6/30/02.
- Clarian Health Partners, Inc., Co-principal Investigator, “In vivo analysis of a human gene therapy protocol designed to enhance chemoresistance in hematopoietic stem cells,” 3/01/00-2/28/02

## **JALEES REHMAN, M.D.**

### **Address:**

Krannert Institute of Cardiology  
Indiana University, School of Medicine  
1800 North Capitol Ave, Room E310  
Indianapolis, IN 46202  
Tel: (317) 962-0074  
Fax: (317) 962-0574

**E-mail:** jrehman@iupui.edu

**Date of Birth:** December 2, 1971

**Languages:** German, English, Urdu and French

### **POSITIONS**

**7/2005 to present**                      **Assistant Professor of Medicine**  
**Indiana University, School of Medicine**

**7/2005 to present**                      **Staff Physician, Division of Cardiology, Department of**  
**Medicine, Indiana University, School of Medicine**

### **EDUCATION & TRAINING**

#### **Postgraduate Education**

7/2001-6/2005                      Cardiology Fellow, Krannert Institute Of Cardiology, Indiana  
University School of Medicine, Indianapolis

6/1999-6/2001                      Internal Medicine Resident, Indiana University, School of  
Medicine, Indianapolis

1/1997-6/1999                      Postdoctoral Research Fellow at the Department of Medicine,  
University of California, San Diego

#### **University Education**

11/1996                              Medical Degree (Aerztliche Pruefung), Technische Universität  
München

11/1992-11/1996                      Medical School of the Technische Universität München, Germany

9/1992                                Physikum (*comparable to a Bachelor degree in pre-clinical sciences*)

11/1990-11/1992                      Medical School of the University of Munich, Germany

#### **Research Interests**

**Biology, physiology and therapeutic potential of stem and progenitor cells in the  
cardiovascular system, the role of inflammation in atherosclerosis and angiogenesis**

**Postgraduate Clinical Experience**

7/2001-6/2005	Cardiology Fellow at the Krannert Institute of Cardiology, Indiana University, School of Medicine
6/1999-6/2001	Residency in Internal Medicine, Indiana University Medical Center

**SCHOLARSHIPS AND AWARDS**

2004	First Prize, Fellows Research Competition IU School of Medicine, Department of Medicine
2003	First Prize, Fellows Research Competition IU School of Medicine, Department of Medicine
1991-1996	Scholar of the German National Scholarship Foundation (Studienstiftung des deutschen Volkes)

**PUBLICATIONS****A. Original articles**

J. Comolli, W. Taylor, **J. Rehman**, and J. W. Hastings (1996) "Regulation of the *Gonyaulax* circadian system by serine/threonine phosphoprotein phosphatases" **Plant Physiology** 111: 285-91

T. Roenneberg and **J. Rehman** (1996), "Nitrate, a non-photic signal for the circadian system" **FASEB Journal** 10: 1443-1447

**J Rehman**, PJ Mills, S Carter, J Chou, J Thomas and AS Maisel (1997) "Dynamic Exercise leads to an Increase in Circulating ICAM-1: Further Evidence for Adrenergic Modulation of Cell Adhesion" **Brain, Behavior, and Immunity** 11: 343-351

AS Maisel, D Cesario, S Baird, **J Rehman**, P Haghghi and SM Carter (1998) "Experimental Autoimmune Myocarditis Produced by Adoptive Transfer of Splenocytes after Myocardial Infarction" **Circulation Research** 82: 458-463

PJ Mills, **J Rehman**, MG Ziegler, SM Carter, JE Dimsdale, AS Maisel (1999): "Nonselective Beta-blockade attenuates the recruitment of CD62L- lymphocytes following exercise" **Eur J Appl Physiol** 79: 6, 531-534

**J Rehman**, JM Dillow, S Carter, J Chou, B Le and AS Maisel (1999) "Increased Production of Antigen-specific immunoglobulins G and M following in vivo treatment with the medicinal plants *Echinacea angustifolia* and *Hydrastis canadensis*" **Immunology Letters** 68: 391-395

PJ Mills, M Goebel, **J Rehman**, MR Irwin, AS Maisel (2000) "Leukocyte adhesion molecule expression and T cell naïve/memory status following isoproterenol infusion" **Journal of Neuroimmunology** 102: 137-144

**J Rehman**, J Li, CM Orschell, KL March (2003) “*Endothelial Progenitor Cells are Derived From Monocyte/Macrophages and Secrete Angiogenic Growth Factors*” ***Circulation*** 107:1164-1169

**J Rehman**, RV Considine, J Bovenkerk, J Li, CA Slavens, R Jones, KL March (2003) “*Obesity Is Associated With Increased Levels of Circulating Hepatocyte Growth Factor*” ***Journal of the American College of Cardiology*** 41: 1408-1413

**J Rehman**, J Li, L Parvathaneni, G Karlsson, VR Panchal, CJ Temm-Grove, J Mahenthiran, KL March (2004) “*Exercise Acutely Increases Circulating Endothelial Progenitor Cells and Monocyte/Macrophage Derived Angiogenic Cells*” ***Journal of the American College of Cardiology*** 43: 2314-8

**J Rehman**, D Traktuev, JL Li, S Merfeld-Clauss, CJ Temm-Grove, JE Bovenkerk, CL Pell, BH Johnstone, RV Considine, KL March (2004) “*Secretion of angiogenic and antiapoptotic factors by human adipose stromal cells*” ***Circulation*** 109 (10): 1292-1298

VR Panchal, **J Rehman**, AT Nguyen, JW Brown, MW Turrentine, Y Mahomed, KL March.(2004) “*Reduced pericardial levels of endostatin correlate with collateral development in patients with ischemic heart disease*” ***Journal of the American College of Cardiology*** 43: 1383-1387

## B. Review articles and Book chapters

T Roenneberg, T. Deng, B Eisensamer, M Mittag, I Neher, **J Rehman** (1995) “*Cellular mechanisms of circadian clocks.*” ***Wiener Medizinische Wochenschrift.*** 145(17-18):385-9.

PJ Mills, MG Ziegler, **J Rehman**, AS Maisel (1997). “Die Rolle adrenerger Mechanismen bei akuten Änderungen der peripheren Lymphozytenverteilung und der Expression von Zelladhäsionsmolekülen” ***Zeitschrift für Medizinische Psychologie***, 2:65-73

T Roenneberg and **J Rehman** (1998) “Survival in a temporal world - the circadian program of the marine unicell *Gonyaulax*” in “**Microbial Responses to Light and Time**”, Editors M. X. Caddick, S. Baumberg, D. A. Hodgson, M. K. Phillips-Jones (Cambridge University Press, Cambridge, UK), pp. 237-250

PJ Mills, MG Ziegler, **J Rehman**, AS Maisel (1998) “*Catecholamines, catecholamine receptors, cell adhesion molecules, and acute stressor-related changes in cellular immunity.*” ***Advances in Pharmacology*** 42:587-90.

**J Rehman** and KL March (2004) “*Adipose Stromal Cell Therapy for Cardiovascular Disease*” in ***Handbook of Cardiovascular Cell Transplantation***, Editors N Kipshidze, P Serruys, Taylor and Francis Publishing

**J Rehman** (2004) “*Can Angiogenesis be Exercised*” in ***Mechansims of Angiogenesis***, Editors M Clauss & G Breier, Birkhäuser Verlag

**J Rehman** and KL March (2005) “*The Biology of Progenitor Cells and Stem Cells in Cardiovascular Disease*” in ***Principles of Molecular Cardiology***, Editors M Runge and C Patterson, Human Press

### C. Relevant Published Abstracts

**J Rehman**, P Mills, JM Dillow, SM Carter, E Bessent, AS Maisel (1998): "Sympathetic activation modulates the pattern of L-selectin expression on circulating monocytes via beta 2-adrenergic mechanisms" **Circulation** 98 (17): 4175 Supp. S

**J Rehman**, J Li, CM Orschell, KL March (2002) "The Expression of Endothelial and Monocytic Adhesion Molecules on Endothelial Progenitor Cells" **Circulation** 106: 730 Supp S

D Traktuev, **J Rehman**, JL Li, EC Judy, CA Slavens, RV Considine, KL March (2003) "Use of adipose stromal cells as autologous cell vectors for nonviral cardiovascular gene therapy" **Molecular Therapy** 7 (5): 601

**J Rehman**, J Li, CA Williams, JE Bovenkerk, RV Considine, KL March (2003) "Angiogenic Potential of Subcutaneous Adipose Stromal Cells for Autologous Cell Therapy" **Journal of the American College of Cardiology** 41 Supplement A: 308 A

JC Howell, **J Rehman**, J Zhong, W Lee, KL March, MC Yoder, EF Srour (2003) "Identification of a common pluripotent stem cell from murine post-natal skeletal muscle and adipose tissue" **Experimental Hematology** 31 Suppl 334

J Case, JC Howell, **J Rehman**, KL March, MC Yoder, EF Srour (2003). "Clonal multilineage differentiation of murine common pluripotent stem cells" **Blood** 102 (11): 747 Part 1

**J Rehman**, J Li, KL March (2003) "Granulocyte Macrophage Colony Stimulating Factor Improves the Survival of Endothelial Progenitor Cells" **FASEB Journal** 99.33

**J Rehman**, J Li, L Parvathaneni, VR Panchal, J Mahenthiran, KL March (2003) "Acute Dynamic Exercise Increases Circulating Endothelial Progenitor Cells" **Journal of the American College of Cardiology** 41 Supplement 296A

G Karlsson, **J Rehman**, HM Meltser, VG Kalaria, JA Breall (2004). "High rate of in-stent thrombosis in cocaine users undergoing coronary stent placement" **Journal of the American College of Cardiology** 43 Supplement 61A

**J Rehman**, R Siddiqui, JL Li, D Traktuev, S Merfeld-Clauss, KL March KL (2004). "Cultured adipose tissue-derived stromal cells express the stem cell marker CD34 and show evidence of differentiation into a cardiomyocyte phenotype" **Journal of the American College of Cardiology** 43 Supplement 177A

### JOURNAL REVIEWER

Ad hoc reviewer for **Circulation**, **Journal of the American College of Cardiology** and the **European Heart Journal**

### GRANT SUPPORT

Showalter Foundation Grant, "The Effects of Polyunsaturated Fatty Acids on Endothelial Progenitor Cells", \$30,000, dates 7/1/2005 to 6/30/2006, Principal Investigator

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed for Form Page 2.  
Follow the sample format on preceding page for each person. **DO NOT EXCEED FOUR PAGES.**

NAME		POSITION TITLE	
Joseph C. Ruiz, Ph.D.		Assistant Professor	
eRA COMMONS USER NAME			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Michigan State University, Lansing, Michigan	B.S.	1982	Microbiology
University of California, San Diego, California	Ph.D.	1988	Biology

**A. PROFESSIONAL EXPERIENCE**

- 1988-1989 Post-Doctoral Research Assistant, Gene Expression Laboratory, The Salk Institute, LaJolla, CA
- 1989-1992 Post-Doctoral Research Assistant, Department of Genetics & Development, Columbia University, New York, NY
- 1992-1994 Post-Doctoral Research Assistant, Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA
- 1994-1999 Assistant Professor, Director of the Wistar Institute Histotechnology Facility, Chairman of the Wistar Institute, IACUC, Director of Summer Undergraduate Internship Program, The Wistar Institute, Philadelphia, PA
- 1997-1999 Adjunct Assistant Professor, Cell and Molecular Biology Graduate Group, University of Pennsylvania, Philadelphia, PA
- 1999-Present Assistant Professor, Wells Center for Pediatric Research, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN
- 2001-Present Secondary Appointment, Assistant Professor, Department of Cellular and Integrative Physiology, Indiana University School of Medicine, Indianapolis, IN
- 2002-2003 Supervisor, In Situ Hybridization Division, Cell and Molecular Biology Core, Indiana University School of Medicine, Indianapolis, IN
- 2002-Present Director, Animal Stem Cell Core, Indiana University School of Medicine, Indianapolis, IN

**B. PUBLICATIONS**

- Ruiz JC & Wahl GM (1986) *Escherichia coli* aspartate transcarbamylase: a novel marker for studies of gene amplification and expression in mammalian cells. *Mol. Cell. Biol.* **6**, 3050-3058.
- Wahl GM, Carroll S, Gaudray P, Meinkoth J & Ruiz JC (1986) Applications of gene transfer in the analysis of gene amplification, pg 289-328. In R. Kucherlapti (ed.), *Gene Transfer*, Plenum Press, New York and London.
- Wahl GM, Lewis KA, Ruiz JC, Rothenberg B, Zhao J & Evans GA (1987) Cosmid vectors for rapid genomic walking, restriction mapping, and gene transfer. *Proc.Natl.Acad.Sci. USA* **84**, 2160-2164.
- Ruiz JC & Wahl GM (1988) Formation of an inverted duplication can be an initial step in gene amplification. *Mol. Cell. Biol.* **8**, 4302-4313.
- Ruiz JC, Choi K, Von Hoff DD, Roninson I & Wahl GM (1989) Autonomously replicating episomes contain *mdr1* genes in a multidrug resistant human cell line. *Mol. Cell. Biol.* **9**, 109-115.
- Ruiz JC & Wahl GM (1990) Chromosomal destabilization during gene amplification. *Mol. Cell. Biol.* **10**, 3056-3066.

Principal Investigator/Program Director (Last, first, middle): Ruiz, Joseph C

Jeannotte L, Ruiz JC & Robertson EJ (1991) Low level of *Hox1.3* gene expression does not preclude the use of promoterless vectors to generate a targeted gene disruption. *Mol. Cell. Biol.* **11**, 5578-5585.

Ruiz JC & Robertson EJ (1994) The expression of the Receptor – Protein Tyrosine Kinase, *eck*, is highly restricted during early mouse development. *Mechanisms of Development* **46**, 87-100.

Ruiz JC, Conlon FL & Robertson EJ (1994) Identification of novel protein kinases expressed in the myocardium of the developing mouse heart. *Mechanisms of Development* **48**, 153-164.

Weinstein DC, Rahman SM, Ruiz JC & Hemmati-Brivanlou A (1996) Embryonic expression of *eph* signaling factors in *Xenopus*. *Mechanisms of Development* **57**, 133-144.

McBride JL & Ruiz JC (1998) Ephrin-A1 is expressed at sites of embryonic blood vessel formation. *Mechanisms of Development* **77**, 201-204.

Mao NC, Steingrimsson E, DuHadaway J, Wasserman W, Ruiz JC, Copeland NG, Jenkins NA & Prendergast, GC (1999) The murine *Bin1* gene functions early in myogenesis and defines a new region of synteny between mouse chromosome 18 and human chromosome 2. *Genomics* **56**, 51-58.

Li B, Ruiz JC & Chun KT (2002) *CUL-4A* is critical for early embryonic development. *Mol. Cell. Biol.* **22**, 4997-5005.

Stephenson A, Nguyen N-T, Huang G-Y, Reuter, S, McBride JL & Ruiz JC (2004) *SNF1LK* encodes a protein kinase that may function in cell cycle regulation *Genomics* **83**, 1105-1115.

Brantley DM, Caughron J, Hicks D, Pozzi A, Ruiz JC & Chen J (2004) EphA2 receptor tyrosine kinase regulates endothelial cell migration and vascular assembly through phosphoinositol 3-kinase mediated Rac1 GTPase activation *J. Cell Science* **117**, 2037-2049.

Ogawa T, Kuwagata M, Ruiz JC & Zhou FC (2005) Differential teratogenic effect of alcohol on embryonic development between C57BL/6 and DBA/2 mice: a new view. *Alcoholism: Clinical and Experimental Research* **29**, 855-863.

Carlone DL, Lee J-H, Young SRL, Dobrata E, Butler JS, Ruiz JC & Skalnik DG (2005) Reduced genomic cytosine methylation and defective cellular differentiation in embryonic stem cells lacking CpG binding protein. *Mol. Cell. Biol.* **25**, 4881-4891.

Ruiz JC (2005) *SNF1LK*, a locus within human chromosome 21q22.3, is expressed during cardiac, skeletal muscle, and lung development (manuscript in review)

### **C. RESEARCH PROJECTS ONGOING OR COMPLETED DURING THE LAST THREE YEARS:**

“Analysis of B61 (ephrin A1) function during vascular development”

Principal Investigator: Joseph Ruiz, Ph.D.

Agency: NHLBI

Grant Number: R29 HL59269

Period: January 10, 1998 – December 31, 2001

Annual Direct Costs: \$70,000

Specific Aims are: 1) Identify *eph* and *ephrin* family members expressed in the developing vascular system by immunohistochemistry; 2) Characterize the defects in vascular development that result from the ablation of ephrin A1 gene expression by gene targeting; 3) Characterize the defects in tumor angiogenesis that result from the ablation of ephrin A1 and/or ephA2, the major ephrin A1 receptor, gene expression by gene targeting.

“Development of a Rodent Resource and Research Center and a Program of Comparative Medicine”

Principal Investigator: Mervin Yoder, MD

Agency: 21<sup>st</sup> Century

Stem Cell Core Director: Joseph C. Ruiz, Ph.D.

Principal Investigator/Program Director (Last, first, middle): Ruiz, Joseph C

Grant Number: 109

Period: 1/29/02-2/29/04

Annual Direct Costs: 5% Salary Support

Specific Aim: Establish a Core Facility dedicated to the derivation of embryonic stem cell lines from “knockout” and transgenic mice.

“Core Centers of Excellence in Molecular Hematology (CCEMH)”

Principal Investigator: Edward Srour, Ph.D. Agency: NIH – NIDDK

Co-Leader, Cell and Molecular Biology Core: Joseph C. Ruiz, Ph.D.

Grant Number: P30 DK49218

Period: 9/1/99-7/31/03

Annual Direct Costs: 5% Salary Support

Specific Aim: Supervise the *in situ* hybridization “division” of the Cell and Molecular Biology Core

“The role of the novel gene SNF1LK in muscle development”

Principal Investigator: Joseph Ruiz, Ph.D. Agency: AHA (Greater Mid-West Affiliate)

Grant Number: 0550023Z

Period: January 1, 2005 – December 31, 2006

Annual Direct Costs: \$66,000

Specific Aims are: 1) define the signaling mechanisms that regulate SNF1LK-mediated cell cycle control; and 2) define the consequences of aberrant SNF1LK signaling during *in vitro* cardiogenesis using transgenic animal and embryonic stem cell models.

**BIOGRAPHICAL SKETCH**

NAME Edward F. Srour		POSITION TITLE Professor of Medicine	
eRA COMMONS USER NAME ESROUR			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
American University of Beirut, Lebanon	B.S.	1979	Agriculture
American University of Beirut, Lebanon	Ingenieur	1979	Argriculture
American University of Beirut, Lebanon	M.S.	1981	Animal Science
University of Illinois, Urbana-Champaign, IL	Ph.D.	1986	Vet. Med. Sci.
Indiana University, Indianapolis, IN	Post Doc	1988	Hem/Onc

**A. Positions and Honors.**

1979 - 1981 Teaching Assistant/Research Assistant: American University of Beirut  
1982 - 1985 Teaching Assistant/Research Assistant: Dep. of Veterinary Pathobiology University of Illinois  
1986 - 1988 Postdoctoral Fellowship: Department of Medicine. Division of Hem/Onc. Indiana University.  
1988 - 1991 Assistant Scientist/Assistant Professor of Medicine. Hematology/Oncology. Indiana University.  
1991 - 1994 Assistant Professor of Medicine: Division of Hematology/Oncology Indiana University.  
1994 - 2000 Associate Professor of Medicine: Division of Hematology/Oncology Indiana University.  
1994 - 2000 Associate Professor of Pediatrics and Microbiology and Immunology Indiana University  
2000 – present Professor of Medicine, Pediatrics and Microbiology and Immunology Indiana University  
1995 - present Adjunct Professor of Biology. Purdue University  
1991 - 2000 Scientific Director, Stem Cell Laboratory  
1988 - present Director, Flow Cytometry Resource Facility.

Agency for International Development; Scholarship: 1976-197

Lebanese National Council for Scientific Research; Scholarship: 1981-1984

American Cancer Society Institutional Research Grant; 7/1988-6/1989 (Principal Investigator)

Biomedical Research Support Grant; Division of Research Resources, NIH 7/19/89-6/1990

American Cancer Society Junior Faculty Research Award; 1/1991 - 12/1993

**B. Selected peer-reviewed publications (in chronological order).**

From >100 peer reviewed articles and 17 book chapters/reviews.

1. Brandt J, Baird N, Lu L, **Srour EF**, Hoffman R. Characterization of a human hematopoietic progenitor cell capable of forming blast cell containing colonies *in vitro*. J of Clinical Investigation. 82(3):1017-1027, 1988.
2. **Srour EF**, Leemhuis T, Brandt JE, van Besien K, Hoffman R. Simultaneous use of Rhodamine 123 phycoerythrin, Texas red and allophycocyanin for the isolation of human hematopoietic progenitor cells. Cytometry. 12(2):179-183, 1991.
3. **Srour EF**, Brandt JE, Leemhuis T, Ballas CB, Hoffman R. Relationship between cell cycle progression and MHC class II antigen expression by primitive human marrow hematopoietic progenitor cells. Journal of Immunology. 148(3):815-820, 1992.
4. **Srour EF**, Zanjani ED, Brandt JE, Leemhuis T, Briddell R, Heerema NA, Hoffman R. Sustained human hematopoiesis in sheep transplanted *in utero* during early gestation with fractionated adult human bone marrow cells. Blood. 79(6):1404-1412, 1992.
5. **Srour EF**, Zanjani ED, Cornetta K, Traycoff C, Flake AW, Hedrick M, Leemhuis T, Hoffman R. Persistence of human multilineage self-renewing lymphohematopoietic stem cells in chimeric sheep. Blood. 82(11):3333-3342, 1993.

6. Traycoff CM, Kosak ST, Grigsby S, **Srouf EF**. Evaluation of the hematopoietic potential of ex vivo expanded marrow and cord blood progenitor cells using cell tracking and limiting dilution analysis. *Blood*. 85(8):2059-2068, 1995.
7. Traycoff CM, Cornetta K, Yoder MC, Davidson A, **Srouf EF**. Ex vivo expansion of murine hematopoietic progenitor cells generates classes of expanded cells possessing varying levels of bone marrow repopulating potentials. *Experimental Hematology*. 24(2):299-306, 1996.
8. Ladd AC, Pyatt R, Gothot A, Grigsby S, McMahel J, Traycoff CM, **Srouf EF**. Orderly process of sequential cytokine stimulation is required for activation and maximal proliferation of primitive human bone marrow CD34+ hematopoietic progenitor cells residing in G<sub>0</sub>. *Blood*. 90(2) 658-668, 1997.
9. Gothot A, Pyatt R, McMahel J, Rice S, **Srouf EF**. Functional heterogeneity of human CD34+ cells isolated in subcompartments of the G<sub>0</sub>/G<sub>1</sub> phase of the cell cycle. *Blood*. 90(11):4384-4393, 1997.
10. Traycoff CM, Orazi A, Grigsby S, Ladd AC, **Srouf EF**. Proliferation-induced decline of primitive hematopoietic progenitor cell activity correlates with an associated increase in the percentage of apoptotic ex vivo expanded CD34+ cells. *Experimental Hematology*. 26(1):53-62, 1998.
11. Veena P, Cornetta K, Williams DA, Traycoff CM, McMahel J, **Srouf EF**. Delayed targeting of cytokine nonresponsive cells with retrovirus mediated gene transfer enhances transduction efficiency and persistence of long-term expression of transduced genes. *Blood*. 91:3693-3701, 1998.
12. Gothot A, Pyatt R, McMahel J, Rice S, **Srouf EF**. Assessment of proliferative and colony-forming capacity after successive in vitro divisions of single human CD34+ cells initially isolated in G<sub>0</sub>. *Experimental Hematology*. 26(7):562-570, 1998.
13. Gothot A, van der Loo JCM, Clapp DW, **Srouf EF**. Cell cycle-related changes in repopulating capacity of human mobilized peripheral blood CD34+ cells in NOD/SCID mice. *Blood*. 92(8):2641-2649, 1998.
14. Abonour R, Williams DA, Einhorn L, Hall K, Chen J, Coffman J, Traycoff CM, Bank A, Kato I, Ward M, Williams SD, Hromas R, Robertson M, Smith FO, Woo, D, Mills B, **Srouf EF**, Cornetta K. Efficient retroviral-mediated MDR-1 gene transfer into autologous human long-term repopulating hematopoietic stem cells. *Nature Medicine*. 6(6):652-658, 2000.
15. Orschell-Traycoff CM, Yoder MC, Hiatt K, Dagher R, **Srouf EF**. Marrow repopulating ability of Sca-1+ Lin-cells fractionated by adhesion molecule expression and position in cell cycle. *Blood*. 96(4):1380-1387, 2000.
16. Wilpshaar J, Falkenburg JHF, Tong X, Noort WA, Breese R, Heilman DK, Kanhai HHH, Traycoff CM, **Srouf EF**. Similar repopulating capacity of mitotically active and resting umbilical cord blood CD34+ cells in NOD/SCID mice. *Blood*. 96(6):2100-2107, 2000.
17. Jetmore A, Plett PA, Tong X, Wolber FM, Breese R, Abonour R, Orschell-Traycoff CM, **Srouf EF**. Homing efficiency, cell cycle kinetics and survival of quiescent and cycling human CD34+ cells transplanted into conditioned NOD/SCID mice. *Blood*. 99(5):1585-1593, 2002.
18. Howell CJ, Yoder MC, **Srouf EF**. Hematopoietic potential of murine skeletal muscle-derived CD45-Sca-1+c-kit- cells. *Experimental Hematology* 30 (8): 915-924, 2002.
19. Broxmeyer HE, **Srouf EF**, Hangoc G, Cooper S, Anderson SA, Bodine DM. High efficiency recovery of functional hematopoietic progenitor and stem cells from human cord blood cryopreserved for 15 years. *Proceedings of the National Academy of Science*. 100(2):645-650, 2003.
20. Howell CJ, Wei-Hua L, Morrison P, Zhong J, Yoder MC, **Srouf EF**. Pluripotent stem cells identified in multiple murine tissues. *Annals of the New York Academy of Science*. 996:158-173, 2003.
21. Li X, Plett PA, Yang Y, Hong P, Freie B, **Srouf EF**, Orschell CM, Clapp DW, Haneline LS. Fanconi anemia type C-deficient hematopoietic stem/progenitor cells exhibit aberrant cell cycle control. *Blood* 102(6):2081-2084, 2003.
22. **Srouf, EF**, Tong X, Sung KW, Plett AP, Rice S, Daggy J, Yiannoutsos CT, Abonour R, Orschell CM. Modulation of in vitro proliferation kinetics and primitive hematopoietic potential of individual CD34+CD38-/lo cells in G<sub>0</sub>. *Blood* 105(8):3109-3116, 2005.
23. Broxmeyer HE, Clapp DW, Orschell CM, Hangoc G, Cooper S, Plett PA, Liles WC, Li X, Graham-Evans B, Calandra G, Bridger G, Dale DC, **Srouf EF**. Rapid Mobilization of Murine and Human Hematopoietic Stem and Progenitor Cells with AMD3100, a CXCR4 Antagonist. *J. Exp Med* 201(8):a307-1318, 2005.
24. Hou Y-H, **Srouf EF**, Ramsey H, Dahl R, Broxmeyer HE, Hromas R. Identification of a Human B-Cell/Myeloid Common Progenitor by the Absence of CXCR4. *Blood* 105(9):3488-3492, 2005.

**C. Research Support.****Ongoing Research Support**

- RO1 HL69156                      Srour EF (PI)                      09/01/01 – 08/31/05  
NIH/NHLBI  
Common Muscle, Hematopoietic and Neural Stem Cells  
The major goal of this project is to investigate the existence of a common or universal pluripotent stem cell in multiple murine tissues and to examine the multilineage differentiation potential of these cells in different tissue microenvironments and conditions.  
Role: PI                              No overlap
- P30 DK49218                      Srour EF (PI)                      09/15/99 - 08/31/05  
NIH/NIDDK  
Core Centers of Excellence in Molecular Hematology  
The major goal of this study is to provide core support for investigators conducting basic and clinical research in hematopoiesis.  
Role: Program Director              No overlap
- P01 HL53586                      Dinauer M (PI)                      07/01/00 – 02/28/05  
   Srour EF (PI, Core A)  
   Srour EF (Co-Inv.Proj  
   1&2)  
NIH/NHLBI  
Gene Replacement Therapy in Hematopoietic Stem Cells  
The major goals of projects 1 and 2 are to examine the utility of different sources of stem cells in gene replacement therapy and to enhance the efficiency of gene transfer into these cells. Core A is a dedicated facility for tissue procurement and analysis of research samples generated in this program.  
Role: PI and Co-Invest.              No overlap
- P30 CA82709                      Williams S (PI)                      07/01/99 – 06/30/05  
NIH/NCI  
Cancer Center Support Grant  
The major goal of this project is to help support the infrastructure costs for the Cancer Center in order to increase the research and clinical activities with in the Center.  
Role: PI (Core)                      No overlap
- HL069669                              Pelus L (PI)                              08/01/01 – 07/31/06  
NIH/NHLBI  
Chemokine Induced Hematopoietic Stem Cell Mobilization  
The major goal of this project is to investigate the potential of different chemokines to mobilize hematopoietic stem cells into the periphery and the effect of these chemokines on stem cell homing  
Role: Co-Invest.                      No overlap
- HL077688                              March K (PI)                              07/01/04 – 06/30/08  
NIH/NHLBI  
Adipose Stromal Cells in Vascular Repair and Hematopoiesis  
The major goal of this project is to investigate the potential of adipose stromal cells to participate in vascular tissue repair in ischemia and to examine the possibility of these cells to differentiate into blood cells under in vivo conditions.  
Role: Co-Invest.                      No overlap

**Pending Research Support**

HL55716-09                      Srour EF (PI)                      04/01/05 – 03/31/10  
 NIH/NHLBI  
 Extrinsic Modulation of Hematopoietic Stem Cell Fate  
 The major goal of this project is to assess the impact of the interaction of stem cells with their hematopoietic microenvironment on stem cell function throughout ontogeny.  
 Role: PI                      No overlap                      **Reviewed 06-17-05: Score 148; percentile 2.8**

AG024940                      Srour EF (PI)                      09/30/04 – 9/29/09  
 NIH/NIA  
 Genomic Instability of the Aging Hematopoietic System  
 The major goal of this project is to prove that senescence of the hematopoietic system results from simultaneous and progressive age-related changes in stem cells and cellular elements of the microenvironment that ultimately disrupt stem cell homeostasis functionally, genetically, and biochemically.  
 Role: PI                      No overlap

P01 HL53586                      Dinauer M (PI)                      07/01/05 – 06/30/10  
    Srour EF (PI, Core A)  
 NIH/NHLBI  
 Gene Replacement Therapy in Hematopoietic Stem Cells  
 The major goals of projects 1 and 2 are to examine the utility of different sources of stem cells in gene replacement therapy and to enhance the efficiency of gene transfer into these cells. Core A is a dedicated facility for tissue procurement and analysis of research samples generated in this program.  
 Role: PI (Core A)                      No overlap                      **To be funded in August 2005**

### **Completed Research Support**

R01 HL62200                      Srour EF (PI)                      04/01/99 - 03/31/03  
 NIH/NHLBI  
 Adhesion Analysis of Cycling Stem Cells Through Ontogeny  
 The major goal of this project was to better understand the mechanisms of homing of HSC during mammalian embryonic development and postnatal trafficking of these cells.  
 Role: PI                      No overlap

RO1 HL55716-08                      Srour EF (PI)                      07/01/00 - 06/30/04  
 NIH/NHLBI  
 Cell Cycle Progression and Hematopoietic Potential  
 The major goal of this project was to characterize the relationship between cell cycle status and cell cycle progression of primitive hematopoietic progenitor cells and their hematopoietic activity and to examine if stem cell proliferation and fate can be modulated in vitro by cytokine stimulation.  
 Role: PI                      No overlap

NAG-1586                      Orschell CM (PI)                      01/01/99 - 12/31/03  
 NASA  
 Self Renewal Replication of Hematopoietic Stem Cells in Microgravity  
 The major goal of this study was to investigate, using the RWV bioreactor, how ex vivo culture under simulated microgravity conditions, coupled with a more architecturally "correct" BM microenvironment, affect cell cycle activation and proliferation of highly purified populations of primitive HPC.  
 Role: Co-Invest.                      No overlap

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## BIOGRAPHICAL SKETCH

Provide the following information for the senior project personnel.  
**DO NOT EXCEED TWO PAGES.**

---

NAME	POSITION TITLE
David L. Stocum	Professor of Biology School of Science Indiana University-Purdue University

---

### Professional Preparation

INSTITUTION AND LOCATION	MAJOR/AREA	DEGREE	YEAR
Susquehanna University, Selinsgrove, PA	Biology and Psychology	B. A.	1961
University of Illinois, Champaign, IL	Zoology	M.S.	1963
University of Pennsylvania, Philadelphia, PA	Cell and Developmental Biology	Ph.D.	1968

### Appointments

1968 – 1990	Assistant Professor through Professor, University of Illinois, School of Life Sciences, Department of Cell and Structural Biology, Champaign, IL
1974 – 1976	Director, Honors Biology Program, University of Illinois, School of Life Sciences, Department of Cell and Structural Biology, Champaign, IL
1984 – 1986	Acting Head, Department of Anatomical Sciences, School of Life Sciences, University of Illinois, Champaign, IL
1984 – 1990	Professor, College of Medicine, University of Illinois
1986 – 1987	Associate in the Center for Advanced Study, University of Illinois, Champaign, IL
1989 – 2004	Professor of Biology and Dean, School of Science, Indiana University-Purdue University Indianapolis, Indianapolis, IN
2004-present	Professor of Biology, School of Science, Indiana University-Purdue University Indianapolis, Director of the Center for Regenerative Biology and Medicine

### Honors and Awards

1988	Singer Medallion for Regeneration Research
1974 – present	AAAS Fellow, Section G (Biological Sciences).

### Selected Publications (of 100 total)

1. Stocum DL 1978 Regeneration of symmetrical hindlimbs in larval salamanders. *Science* 200: 790-793.
2. Nardi JB, Stocum DL 1983 Surface properties of regenerating limb cells: evidence for gradation along the proximodistal axis. *Differentiation* 25:27-31.
3. Crawford K, Stocum D L 1988 Retinoic acid coordinately proximalizes regenerate pattern and blastema differential affinity in axolotl limbs. *Development* 102: 687-698.

4. Stocum D L 1995 Wound Repair, Regeneration and Artificial Tissues. Austin: RG Landes Co, 221 pp.
5. Stocum, D.L. 1998 Bridging the Gap: Restoration of Structure and Function in Humans. In: Cellular and Molecular Basis of Regeneration: From Invertebrates to Humans. P. Ferretti and J. Geraudie, eds., John Wiley and Sons, Ltd., pp.411-490.
6. Stocum, D.L. 1998 Regenerative biology and engineering: strategies for tissue restoration. Wound Repair and Reg. 6: 276-290.
7. Stocum, D.L. 1999 Regenerative biology: a millennial revolution. Sem. Cell & Dev Biol 10: 433-440.
8. \*Stocum D. L. 2001 Regenerative biology and medicine: a new era in bioengineering. Cardiac and Vasc Reg 1:157-169.
9. Stocum DL 2002 Stem cells in regenerative biology and medicine. Wound Rep Reg 94:29- 42.
10. \*Nye HLD, Cameron JA, Chernoff EG, Stocum DL 2003 Regeneration of the urodele limb: a review. Dev Dynam 226:280-294.
11. Chernoff EAG, Stocum DL, Nye HLD, Cameron JA 2003 Urodele spinal cord regeneration and related processes. Dev Dynam 226:295-307.
12. \*King MW, Nguyen T, Calley J, Harty MW, Muzinich MC, Mescher AL, Chalfant C, N'Cho M, McLeaster K, McEntyre J, Stocum DL, Smith RC, Neff AW (2003) Identification of genes expressed during *Xenopus laevis* limb regeneration by using subtractive hybridization. Dev Dynamics 226:398-409.
13. Stocum DL 2003 Stem cells in amphibian regeneration. In: Stem Cell Handbook. Sell S, ed. Humana Press, Towota, NJ, pp 89-100
14. Stocum DL 2004 Amphibian regeneration and stem cells. In Regeneration: Beyond the Stem Cells. Heber-Katz E (ed). Springer Verlag, Heidelberg, pp 1-70.
15. Stocum DL 2004 Tissue Restoration Through Regenerative Biology and Medicine. Adv in Anat, Embryol and Cell Biol 176:1-104.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Michael Sturek		POSITION TITLE	
eRA COMMONS USER NAME MSTUREK		Professor and Chair	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Augustana College, Rock Island, IL	B.A.	1979	Exercise Physiology, Psychol.
Purdue University, West Lafayette, IN	M.S.	1980	Exercise Physiology
University of Iowa, Iowa City, IA	Ph.D.	1985	Pharmacology
University of Chicago	Postdoc.	1986-1988	Membrane Physiology

**NOTE: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.**

**A. Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

**Professional Positions**

1980-1983 NIH Predoctoral Research Trainee, Exercise Science Program, University of Iowa  
 1982-1983 Assistant Laboratory Director and Instructor, Exercise Science Program, University of Iowa  
 1983-1986 NIH Predoctoral Research Trainee, Department of Pharmacology, University of Iowa  
 1986-1987 NIH Postdoctoral Fellow, Dept. Pharmacol. & Physiological Sciences, University of Chicago  
 1987 Research Associate, Department of Pediatrics, University of Chicago  
 1987-2000 Research Investigator, Dalton Cardiovascular Research Center, University of Missouri  
 1987-1993 Assistant Professor, Department of Physiology, School of Medicine, Univ. of Missouri  
 1993-1999 Associate Professor, Department of Physiology, School of Medicine, Univ. of Missouri  
 1999-2004 Professor, Dept. of Medical Pharmacology & Physiology, School of Medicine, Univ. of Missouri  
 2000-2004 Professor of Internal Medicine, School of Medicine, Univ. of Missouri  
 2002-2004 Associate Director of Basic Research, Center for Diabetes & Cardiovascular Health, U. Missouri  
 2004- Professor and Chair, Dept. of Cellular & Integrative Physiology, Indiana U. School of Medicine

**Awards, Honors, and Professional Activities (selected)**

1992 Program Project Site Visit for NIH NHLBI Research Review Committee B  
 1992, 1995-6 Cardiovascular Study Section A, Division of Research Grants, NIH, Ad-Hoc reviewer  
 1993,95,98,99 Experimental Cardiovascular Sciences Study Section, NIH, Special Reviewer  
 1997, 1998 Physiology Study Section, NIH, Special Reviewer  
 1999 Comparative Medicine Study Section, NIH, Special Reviewer  
 1993-1998 Research Career Development Award, NIH  
 1999 American Diabetes Association Award for Outstanding Community Service In *Reaching People*  
 2002-2003 President, American Diabetes Association, South Central Region  
 2004 Special Review Committee for Program Project Grant, NIH NHLBI  
 2000-2004 Vascular Cell and Molecular Biology Study Section, NIH, Regular Member

**B. Selected peer-reviewed publications (in chronological order).** Do not include publications submitted or in preparation.

**Manuscripts relevant to the proposal (selected after 2002 from a total of 97; 198 abstracts)**

- Ojuka, E.O., T.E. Jones, L.A. Nolte, M. Chen, B.R. Wamhoff, M. **Sturek**, and J.O. Holloszy. Regulation of GLUT4 biogenesis in muscle: evidence for involvement of AMPK and Ca<sup>2+</sup>. *Am. J. Physiol.:Endocrinol. Metab.* 282:E1008-E1013, 2002.
- Wamhoff, B.R., J.L. Dixon, and M. **Sturek**. Atorvastatin treatment prevents alterations in coronary smooth muscle nuclear Ca<sup>2+</sup> signaling associated with diabetic dyslipidemia. *J. Vasc. Res.* 39:208-220, 2002.
- Hainsworth, D.P., M.L. Katz, D.A. Sanders, D.N. Sanders, E.J. Wright, and M. **Sturek**. Retinal capillary basement membrane thickening in a porcine model of diabetes mellitus. *Comp. Med.* 52:523-529, 2002.

5. Ojuka, E.O., T.E. Jones, D-H. Han, M. Chen, B.R. Wamhoff, M. **Sturek**, and J.O. Holloszy. Intermittent increases in cytosolic Ca<sup>2+</sup> stimulate mitochondrial biogenesis in muscle cells. *Am. J. Physiol.:Endocrinol. Metab.* 283:E1040-E1045, 2002.
5. Dixon, J.L., S. Shen, J.P. Vuchetich, E. Wysocka, G. Sun, and M. **Sturek**. Increased atherosclerosis in diabetic dyslipidemic swine: protection by atorvastatin involves decreased VLDL triglycerides but minimal effects on the lipoprotein profile. *J. Lipid Res.* 43:1618-1629, 2002.
6. Wamhoff, B.R., D.K. Bowles, N.J. Dietz, Q. Hu, and M. **Sturek**. Exercise training attenuates coronary smooth muscle phenotypic modulation and nuclear Ca<sup>2+</sup> signaling. *Am. J. Physiol.: Heart Circ. Physiol.* 283:H2397-H2410, 2002.
7. Seye, C.I., Q. Kong, L. Erb, R.C. Garrad, B. Krugh, M. Wang, J.T. Turner, M. **Sturek**, F.A. Gonzalez, and G.A. Weisman. Functional P2Y<sub>2</sub> nucleotide receptors mediate uridine 5'-triphosphate-induced intimal hyperplasia in collared rabbit carotid arteries. *Circulation* 106:2720-2726, 2002.
8. Hill, B.J.F. and M. **Sturek**. Pharmacological characterization of a UTP-sensitive P2Y nucleotide receptor in organ cultured coronary arteries. *Vasc. Pharmacol.* 39:83-88, 2002.
9. Boullion, R.D., E.A. Mokolke, B.R. Wamhoff, C.R. Otis, J. Wenzel, J.L. Dixon, and M. **Sturek**. Porcine model of diabetic dyslipidemia: insulin and feed algorithms for mimicking diabetes mellitus in humans. *Comp. Med.* 53:42-52, 2003.
10. Otis, C.R., B.R. Wamhoff, and M. **Sturek**. Hyperglycemia-induced insulin resistance in diabetic dyslipidemic Yucatan swine. *Comp. Med.* 53:53-64, 2003.
11. Hill, B.J.F., E.M. Price, J.L. Dixon, and M. **Sturek**. Increased calcium buffering in coronary smooth muscle cells from diabetic dyslipidemic pigs. *Atherosclerosis* 167:15-23, 2003.
12. Lee, D.L., B.R. Wamhoff, L.C. Katwa, H.K. Reddy, D.J. Voelker, J.L. Dixon, and M. **Sturek**. Increased endothelin-induced Ca<sup>2+</sup> signaling, tyrosine phosphorylation, and coronary artery disease in diabetic dyslipidemic swine are prevented by atorvastatin. *J. Pharmacol. Exp. Ther.* 306:132-140, 2003.
13. Laughlin, M.H., W.V. Welshons, M. **Sturek**, J.W.E. Rush, J.R. Turk, J.A. Taylor, B.M. Judy, K.K. Henderson, and V.K. Ganjam. Gender, exercise training, and eNOS expression in porcine skeletal muscle arteries. *J. Appl. Physiol.* 95:250-264, 2003.
14. Mokolke, E.A., Q. Hu, M. Song, L. Toro, H.K. Reddy, and M. **Sturek**. Altered functional coupling of coronary K<sup>+</sup> channels in diabetic dyslipidemic pigs is prevented by exercise. *J. Appl. Physiol.* 95:1179-1193, 2003.
15. Turk, J.R., J.A. Carroll, M.H. Laughlin, T.R. Thomas, J. Casati, D.K. Bowles, and M. **Sturek**. C-reactive protein correlates with macrophage accumulation in coronary arteries of hypercholesterolemic pigs. *J. Appl. Physiol.* 95:1301-1304, 2003.
16. Reddy, H.K., S.K. Koshy, J. Foerst, and M. **Sturek**. Remodeling of coronary arteries in diabetic patients – an intravascular ultrasound study. *Echocardiography* 21:139-144, 2004.
17. Witczak, C.A. and M. **Sturek**. Exercise prevents diabetes-induced impairment of superficial buffer barrier in porcine coronary smooth muscle. *J. Appl. Physiol.* 96:1069-1079, 2004.
18. Heaps, C.L., J.L. Parker, M. **Sturek**, and D.K. Bowles. Altered calcium sensitivity contributes to enhanced contractility of collateral-dependent coronary arteries. *J. Appl. Physiol.* 97:310-316, 2004.
19. Shen, J., C.I. Seye, M. Wang, G.A. Weisman, P.A. Wilden, and M. **Sturek**. Cloning, upregulation, and mitogenic role of porcine P2Y<sub>2</sub> receptor in coronary artery smooth muscle cells. *Mol. Pharmacol.* 66:1265-1274, 2004.
20. Korte, F.S., E.A. Mokolke, M. **Sturek**, and K.S. McDonald. Exercise improves impaired ventricular function and alterations of cardiac myofibrillar proteins in diabetic dyslipidemic pigs. *J. Appl. Physiol.* 98:461-467, 2005.
21. Mokolke, E.A., N.J. Dietz, D.M. Eckman, M.T. Nelson, and M. **Sturek**. Diabetic dyslipidemia and exercise affect coronary tone and differential regulation of conduit and microvessel K<sup>+</sup> current. *Am. J. Physiol.: Heart Circ. Physiol.* 288:H1233-1241, 2005.
22. Shen, J., S.P. Halenda, M. **Sturek**, and P.A. Wilden. Novel mitogenic effect of adenosine on coronary artery smooth muscle cells: role for the A<sub>1</sub> adenosine receptor. *Circ. Res.* 96:982-990, 2005.
23. Witczak, C.A. and M. **Sturek**. Training-induced sarcoplasmic reticulum Ca<sup>2+</sup> unloading occurs without Ca<sup>2+</sup> influx. *Med. Sci. Sports Exercise* 37:1119-1125, 2005.
24. Shen, J., S.P. Halenda, M. **Sturek**, and P.A. Wilden. Cell signaling evidence for adenosine stimulation of coronary smooth muscle proliferation via the A<sub>1</sub> adenosine receptor. *Circ. Res.* 97:574-582, 2005.

**C. Research Support.** List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

**STUREK, M.**

**COMPLETED**

Sturek (PI) 12/00-12/02  
Pharmacia Corporation  
COX-2 inhibitors in anti-atherogenic therapy and COX-2 gene transfer  
Major goals: Determine whether the cyclooxygenase-2 (COX-2) inhibitor, SC236, will prevent atherosclerosis in type 2 diabetic pigs. Conversely, we will determine whether over-expression of the COX-2 gene via adenoviral vectors directly in the coronary artery via local delivery catheters will increase atherosclerosis/restenosis.

P01 HL52490-08 (Laughlin, PI) 5/00-5/05 (terminated role after leaving U. of Missouri)  
NIH/NHLBI Project 1 5/00-5/01 only  
Core B (Animal Core)  
Vascular cell biology: exercise training & coronary disease  
Project 1 – Ion channels, Ca<sup>2+</sup> and exercise: coordinated regulation of myogenic tone  
Major goals: Project 1 – The roles of hyperlipidemia, protein kinase c, gender, and exercise training in modulation of voltage-gated Ca channels and myogenic tone are determined in pig coronary artery smooth muscle. Core B (Animal Core) – Characterize porcine models of hyperlipidemia by *in vivo* intravascular ultrasound, coronary blood flow velocity, lipids, etc.

Sturek (PI) 6/03-6/05  
American Diabetes Association  
Coronary artery disease in a swine model of the metabolic syndrome  
Major goals: Determine coronary artery disease in the obese Ossabaw pig compared to lean controls. Characterize the metabolic syndrome in obese pigs by: 1) visceral obesity, 2) glucose intolerance and insulin resistance, 3) dyslipidemia (increased LDL/HDL cholesterol and triglycerides), and 4) hypertension.

**ONGOING**

R24 RR13223-07 (Sturek, PI) 5/03-5/08  
NIH/NCRR  
Porcine models of coronary artery disease in diabetes  
Major goals: Characterize porcine models of diabetes (metabolic syndrome [pre-diabetes], type 1, and type 2) using metabolic, endocrine, and cardiovascular criteria. More extensive atherosclerosis and coronary stenting will be studied. These studies provide an animal resource for numerous investigators, including funded project HL62552 (below).

R01 HL62552-06 (Sturek, PI) 9/03-9/07  
NIH/NHLBI  
Exercise, diabetes, and coronary smooth muscle Ca<sup>2+</sup>  
Major goals: Determine nuclear Ca signaling, tyrosine phosphorylation, and K channel mechanisms underlying the coronary smooth muscle adaptations in macro- and microvasculature in diabetic dyslipidemic pigs after more extensive atherosclerosis, coronary stenting, and exercise training.

T35 HL07802-12 (Sturek, PI) 8/05-8/10  
NIH/NHLBI  
Short-term training for minority students  
Major goals: Provide research training for undergraduate minority students during the summer months. Training includes direct laboratory research, advisement on career opportunities, and ethics.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed on Form Page 2.  
Follow the sample format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Mervin C. Yoder, M.D.		POSITION TITLE Professor of Pediatrics and of Biochemistry and Molecular Biology		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)				
INSTITUTION AND LOCATION		DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Malone College, Canton, OH		B.A.	1975	Biology
Indiana State University, Terre Haute, IN		M.A.	1976	Physiology
Indiana University School of Medicine, Indianapolis, IN		M.D.	1980	Medicine

**A. Positions and Honors****Positions and Employment**

- 1985-1991 Assistant Professor of Pediatrics, Indiana University School of Medicine, Indianapolis, IN  
 1990-1991 Assistant Professor of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, IN  
 1991-2000 Associate Professor of Pediatrics and of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, IN  
 2000-pres. Professor of Pediatrics and of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, IN

**Honors**

- 1997 Teaching Excellence Recognition Award, Indiana University School of Med., Indianapolis, IN  
 1998 Perinatal Research Society  
 2001 American Pediatric Society  
 2003 Richard and Pauline Klingler Professor of Pediatrics

**B. Selected peer-reviewed pertinent publications.**

(pertinent publications from &gt; 140)

1. Yoder MC, Du X-X, Williams DA: High proliferative potential colony-forming cell heterogeneity identified using counterflow centrifugal elutriation. *Blood* 82(2):385-391, 1993.
2. Yoder MC, Papaioannou VE, Breitfeld PP, Williams DA: Murine yolk sac endoderm- and mesoderm-derived cell lines support in vitro growth and differentiation of hematopoietic cells. *Blood* 83(9):2436-2443, 1994.
3. Yoder MC, King B, Hiatt K, Mukherjee P, Williams DA: Growth of bone marrow high proliferative potential colony forming cells during in vitro co-culture with murine embryonic yolk sac cell lines. *Blood* 86:1322-1330, 1995.
4. Yoder MC, Cumming J, Hiatt K, Mukherjee P, Williams DA: A novel method of myeloablation to enhance engraftment of adult bone marrow cells in newborn mice. *Biol Blood Marrow Transplant* 2:59-67, 1996.
5. Leemhuis T, Yoder MC, Grigsby S, Eder P, Srouf EF: Isolation of primitive human bone marrow hematopoietic progenitor cells using Hoechst 33342 and rhodamine 123. *Exp Hematol* 24:1215-1224, 1996.
6. Dutt P, Hanenberg H, Vik T, Williams DA, Yoder MC: A recombinant human fibronectin fragment facilitates retroviral mediated gene transfer into human hematopoietic progenitor cells. *Biochem Mol Biol Internat* 42(5):909-917, 1997.
7. Yoder MC, Hiatt K: Engraftment of embryonic hematopoietic cells in conditioned newborn recipients. *Blood* 89:2176-2183, 1997.
8. Yoder MC, Hiatt K, Mukherjee: In vivo repopulating hematopoietic stem cells are present in the murine yolk sac at day 9.0 postcoitus. *Proc Natl Acad Sci USA* 94:6776-6780, 1997.
9. Yoder MC, Hiatt K, Dutt P, Mukherjee P, Bodine DM, Orlic D: Characterization of definitive lymphohematopoietic stem cells isolated from the day 9 murine yolk sac. *Immunity* 7:335-344, 1997.

10. Ponnazhagan S, Wang X-S, Kurpad C, Yoder MC, Srour EF, Srivastava A: Adeno-associated virus 2-mediated transduction of primary human bone marrow-derived CD34<sup>+</sup> hematopoietic cells: Donor variation and correlation of expression with cellular differentiation. *J Virol* 71(11): 8262-8267, 1997.
11. Orlic D, Girard LJ, Anderson SM, Pyle LC, Yoder MC, Broxmeyer HE, Bodine DM: Identification of human and mouse hematopoietic stem cell (HSC) populations expressing high levels of mRNA encoding retrovirus receptors. *Blood* 91(9): 3247-3254, 1998.
12. Dagher R, Hiatt K, Traycoff C, Srour E, Yoder MC: c-Kit and CD38 are expressed by reconstituting hematopoietic cells present in the murine yolk sac. *Biol Blood Marrow Transplant* 4:69-74, 1998.
13. Haneline LS, Gobbett TA, Ramani R, Carreau M, Buchwald M, Yoder MC, Clapp DW. Loss of FancC function results in decreased hematopoietic stem cell repopulating ability. *Blood* 94(1):1-9, 1999.
14. Orschell-Traycoff CM, Hiatt K, Dagher RN, Rice S, Yoder MC, Srour EF: Homing and engraftment potential of Sca-1<sup>+</sup>Lin<sup>-</sup> cells fractionated on the basis of adhesion molecule expression and position in cell cycle. *Blood* 96(4):1380-1387, 2000.
15. Palis J, Chan, RJ, Koniski A, Patel R, Starr M, Yoder MC: Spatial and temporal emergence of high proliferative potential hematopoietic precursors during murine embryogenesis. *Proc Natl Acad Sci USA* 98(8): 4528-4533, 2001.
16. Badylak SF, Park K, Peppas N, McCabe G, Yoder MC: The composition of bioscaffolds affects in-vivo cell recruitment and alters the pattern of tissue repair. *Exp Hematol* 29(11):1310-1318, 2001.
17. Xie X, Chan RJ, Starr M, Johnson SA, Li W, Morrison P, Yoder MC. Thrombopoietin promotes mixed-lineage and megakaryocytic colony forming unit growth but inhibits primitive and definitive erythropoiesis in cells isolated from the early yolk sac. *Blood* 101(4):1329-1335, 2003.
18. Ingram DA, Huddleston H, Tan B, Yang FC, Wenning MJ, Orazi A, Yoder MC, Kapur R: A functional *p85* gene is required for normal murine fetal erythropoiesis. *Blood* 102(1):142-145, 2003
19. Guo Y, Chan R, Ramsey H, Li W, Xie X, Shelley WC, Martinez-Barbera JP, Bort B, Zaret K, Yoder MC, Hromas R. The homeoprotein Hex is required for hemangioblast differentiation. *Blood* 102(7):2428-2435, 2003
20. Chan RJ, Johnson SA, Li Y, Yoder MC, Feng GS. A definitive role of Shp-2 tyrosine phosphatase in mediating embryonic stem cell differentiation and hematopoiesis. *Blood* 102(6):2074-2080, 2003
21. Ferkowicz M, Li W, Starr M, Xie X, Morrison P, Johnson S, Shelley C, Yoder MC. CD41 expression defines the onset of primitive and definitive hematopoiesis in the mouse embryo. *Development* 130(18):4393-4403, 2003
22. Li W, Johnson SA, Shelley WC, Ferkowicz M, Morrison P, Li Y, Yoder MC. Primary endothelial cells isolated from the yolk sac and paraaortic splanchnopleure (P-Sp) support the expansion of adult marrow stem cells in vitro. *Blood* 102(13): 4345-4353, 2003
23. Ingram DA, Mead LE, Tanaka H, Meade V, Fenoglio A, Mortell K, Pollok K, Ferkowicz MJ, Gilley D, Yoder MC. Identification of a novel hierarchy of human endothelial progenitor cells utilizing a clonogenic assay. *Blood* 104(9): 2752-2760, 2004
24. Yoder MC. Generation of embryonic HSCs and assays to detect them. *Oncogene* 23:7161-7163, 2004
25. Baumann CI, Bailey AS, Li W, Ferkowicz MJ, Yoder MC, Fleming WH. PECAM-1 is expressed on hematopoietic stem cells throughout ontogeny and identifies a population of erythroid progenitors. *Blood* 104(4): 1010-1016, 2004
26. Li Y, McClintick J, Zhong L, Edenberg HJ, Yoder MC, Chan RJ. Murine embryonic stem cell differentiation is promoted by SOCS-3 and inhibited by the zinc finger transcription factor Klf4. *Blood* 105:635-637, 2004
27. Johnson SA and Yoder MC. Reconstitution of hematopoiesis following transplantation into neonatal mice, in Baron MH (ed): *Methods in Molecular Medicine, Vol. 105: Developmental Hematopoiesis; Methods and Protocols*, Humana Press, Totowa, NJ, 2004, pp. 95-105
28. Ingram DA, Mead LE, Moore DB, Woodard W, Fenoglio A, Yoder MC. HUVECs rapidly proliferate because they contain a complete hierarchy of endothelial progenitor cells. *Blood* 105:2783-2786, 2005
29. Li W, Ferkowicz M, Johnson SA, Shelley WC, Yoder MC. CD41 expression discriminates hematopoietic from endothelial cells in early murine yolk sacs. *Stem Cells Development* 14:8-19, 2005
30. Kondo T, Johnson SA, Yoder MC, Romand R, Hashino E. Sonic hedgehog and retinoic acid synergistically promote sensory lineage specification from bone marrow-derived pluripotent stem cells. *Proc Natl Acad Sci USA* 102(13): 4789-4794, 2005.
31. Zou G-M, Chen J-J, Yoder MC, Wu W, Rowley JD. Knockdown of PU.1 by small interfering RNA in CD34<sup>+</sup> embryoid body cells derived from mouse ES cells turns cell fate determination to pro-B cells. *Proc Natl Acad Sci USA* 102: 13236-13241, 2005

32. Ingram DA, Yoder MC. Unresolved questions, changing definitions, and novel paradigms for defining endothelial progenitor cells. *Blood* 106:1525-1531, 2005

### **Research projects ongoing**

#### Ongoing work

R01HL63169 (Yoder, P.I.) 7/1/99-3/31/09 30%  
 NIH \$372,465 (direct/yr)  
 Endothelial cell role in yolk sac stem cell development

The major goal of this application is to study endothelial and stem cell development in the murine yolk sac. Competitive renewal of this grant received priority score of 156 (8<sup>th</sup> percentile: 7/1/04-6/30/09).

P60 HL 53586 (Dinauer, P.I.) 7/1/05-6/30/10 10%  
 NIH (Yoder, Co-P.I. on Proj. 2) \$210,210 (direct/yr)  
 Gene Replacement Therapy in Hematopoietic Stem Cells

The major goal of Project 2 is to examine novel methods of myeloablation in transplant settings using gene corrected hematopoietic stem cells.

P50 DK61594 (Molitoris, P.I.) 6/1/02 – 5/37/07 5%  
 NIH (Yoder, Co-Invest, Project 3) \$118,549 (direct/yr)  
 Center for advance renal microscopic analysis (Project 3)

The major goal of this project is to develop transgenic animals expressing endothelial specific proteins.

R01 HL77688-01 (March, P.I.) 7/1/04-6/30/08 5%  
 NIH (Yoder, Co-Investigator) Total direct costs, \$1,250,000

The major goal of this project is to analyze adipose stromal cell differentiation into hematopoietic cells.

R01 HL75783-01A1 (Hromas, P.I.) 7/1/04-6/30/08 5%  
 NIH (Yoder, P.I. of Indiana University Subcontract) Total subcontract direct costs, \$266,000

The major goal of this project is to analyze differentiation of mesoderm cells in ES and embryos lacking the transcription factor Hex.

### **Research completed in past 3 years**

R01 HL 63219 (Clapp, P.I.) 9/1/00 – 8/31/05  
 NIH (Yoder, Co, P.I.)  
 Hematopoiesis and Leukemic Transformation in *Fac* Mice.

The major goal of this application is to develop aplastic and leukemogenic models of Fanconi anemia using *Fancc* <sup>-/-</sup> mice.

R01 HL69156 (Srour, P.I.) 9/30/01 – 8/31/05  
 NIH (Yoder, Co-Invest)  
 Common muscle, hematopoietic, and neural stem cells

Principal Investigator/Program Director (Last, first, middle): \_\_\_\_\_

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The major goal of this application is to determine whether a stem cell with a particular cell surface phenotype resides in multiple tissues and exhibits the capacity to give rise to many different tissues in vivo upon.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed for Form Page 2.  
Follow sample format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME		POSITION TITLE		
Feng C. Zhou, Ph.D.		Professor of Anatomy/Cell Biology & Neurobiology		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)				
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY	
National Taiwan Normal University/ Taiwan	B.S.	1975	Biology	
City University of New York	M.Phil	1981	Anatomy	
Mt. Sinai School of Medicine/ New York	Ph.D	1983	Neuroanatomy	
New York University	Post-Doc.	1983-1985	Neurobiology	

**A. Positions and Honors.**

7/1983-7/1985 Assistant Professor of Anatomy, New York College, Podiatric Medicine  
 8/1984-7/1987 Adjunct Assistant Professor of Biology, New York University  
 7/1985-7/1987 Assistant Research-Anatomist, UCLA, School of Medicine  
 7/1987-6/1991 Assistant Professor of Anatomy and Medical Neurobiology, Indiana Univ. Sch. Med.  
 7/1991-6/1997 Associate Professor of Anatomy and Medical Neurobiology, tenured, Indiana Univ. Sch. Med.  
 7/1997-present Professor of Anatomy/ Cell Biology and Medical Neurobiology, Indiana Univ. Sch. Med.

**Editorial Board**

1/2000-12/2002, Experimental Neurology: Editorial Board Member  
 1/2003-Present Current Neurovascular Research: Editorial advisory Board Member,  
 4/2005-present Recent Patent Review on CNS Drug Discovery: Editorial Advisory Board Member

**B. Selected peer-reviewed publications). [Of 74 total peer-reviewed articles and 10 book chapters]**

Zhou, F.C. and Chiang, Y. S. (1995) Excitotoxins induced trophic bridging directs axonal growth of Zhou, F.C., Azmitia, E.C., Bledsoe, S. (1995) Rapid serotonergic fiber sprouting in response to ibotenic acid lesion in the striatum and hippocampus. *Develop. Brain Res.* 80,89-98.  
 Zhou, F.C., Lumeng, L., and Li, T.-K. (1995) Quantitative immunocytochemical evaluation of serotonergic innervation in alcoholic rat brain. *Neurochem. International*, 26,135-143.  
 Zhou, F.C., Zhang, J.K., Lumeng, L., and Li, T.-K. (1995) Mesolimbic dopamine system in alcohol-preferring rats, *Alcohol*, 12, 403-412. transplanted neurons to distal target. *Cell Transplantation*. 4, 103-112.  
 Patel, D.T. Azmitia, E.C. and Zhou, F.C., (1996) Increased 5-HT<sub>1a</sub> receptor immunoreactivity in the rat hippocampus following 5,7-DHT lesions in the cingulum bundle and fimbria-fornix. *Behavioral Brain Res.* 73:319-323.  
 Zhou F.C., Xu, Yi, Bledsoe, S., Lin, R., and Kelley, M. R. (1996) Serotonin transporter antibodies: production, characterization, and localization in the brain, *Molecular Brain Res.* 43: 267-278.  
 Zhou, F. C. and Bledsoe, S. (1996) Methamphetamine causes rapid varicosity, perforation and definitive degeneration of serotonin fibers: an immunocytochemical study of serotonin transporter, *Neuroscience-Net*, V.1, Article 10009, Oct. 28, 1996, <http://www.neuroscience.com/>.  
 Zhou, F.C., Chiang, Y. H., and Wang, Y. (1996) Constructing a new nigrostriatal pathway in the parkinsonian model with bridged neural transplantation in substantia nigra. *J. Neurosci.* 16, 6965-6974.  
 Wang, Y. Chiou, A.L. Wang, S.D., Chen, L.-K. Chen, J.F., and Zhou, F.C. (1997) Transplantation of microencapsulated PC12 cells provides long-term improvement of dopaminergic functions in hemiparkinsonian rats. *Chinese Journal of Physiology*, 40:12-129.  
 Tang, F.Y., Zhou, F.C., Chiou, A.L. Chen, L.-K. Wang, Y. (1998) Intranigral ventral mesencephalic grafts and nigrostriatal injection of GDNF restore dopamine in the striatum of 6-OHDA-lesioned rats. *Exp Brain Res.* 119(3):287-296.  
 Zhou, F. C., and Chiang, Y. H. (1998) Long-term non-passaged EGF-responsive neural precursor cells are stem cells. *Wound Repair & Regeneration*, 6:337-348

- Zhou, F.C., Makinzie, D.L., Patel, T.D., Lumeng, L., and Li, T.-K. (1998) Additive reduction of alcohol drinking by 5-HT<sub>1A</sub> antagonist WAY100635 and serotonin uptake blocker fluoxetine in alcohol-preferring P rats. *Alcoholism: Clin. Exp. Res.* 22: 266-269.
- Zhou, F. C., Tao-Cheng, J.-H., Segu, L., Patel, T., and Wang, Y. (1998) Serotonin transporters are located on the axons beyond the synaptic junctions: anatomical and functional evidence. *Brain Res.* 805:241-254.
- Zhou, F.C., Patel, T.D., Swartz, D., Xu, Y. & Kelley, M.R. (1999) Production and characterization of an anti-5-HT<sub>1A</sub> receptor antibody which detects functional 5-HT<sub>1A</sub> binding sites. *Brain Res Mol Brain Res.* 69:186-201
- Tao-Cheng J.-H. and F. C. Zhou (1999) Differential polarization of serotonin transporters in axons versus somatodendrites: an immunogold electron microscopy study, *Neurosci.* 94:821-830.
- Zhou F.C., Sari Y., Zhang J.K. (2000) Expression of serotonin transporter protein in developing rat brain. *Brain Res Dev Brain Res.* 119(1):33-45
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### C. Research Support

#### Ongoing Research Support

UO1 AA14819 (Goodlett/Zhou) 10/1/03-9/30/06 14%

NIH/NIAAA

“Testing FASD Therapeutic Agents in Rodent Model”

The goal of this study is to test the synthetic bioactive peptides analogue to the brain neurotrophic and neuroprotective factors on treatment of fetal alcohol induced brain growth deficit.

Role : Co-principal investigator.

PHS P50 AA0761 Crabb (Zhou, Component PI 12/1/02- 11/31/07 13%

NIH/NIAAA

“Alcohol Research Center: Center on Genetic Determinants of Alcohol Ingestion”

Component --Pharmacogenetics of Fetal Alcohol Syndrome

Examine the genes and biology of the alcohol related neurodevelopmental deficit in an embryonic culture and in vivo model. Identify the genes that mediate the individual differential sensitivity.

Role: Component PI

Indiana State Research Fund (Nelson) 9/1/04-8/31/07 10%

Co-investigator (Zhou)

“Head and spinal cord injury”

Investigate the spinal cord injury and CNS damage after spinal transection and contusion in rat model. Cellular therapy with transplantation of neural stem cells.

#### Completed Research Support in the Last Three Years

NIH R01AA12406 Zhou (PI) 3/1/00-2/28/05 30%

NIH/NIAAA

“Alcohol and Brain Development: A Cascaded Midline Hypothesis”

The goal of this project is to investigate a midline hypothesis of fetal alcohol syndrome. A midline structural and a monoamine neural defects together undermine a cascaded deficit in brain development. Explore neurotrophic factors for their protection against the alcohol's dysmorphogenesis.

UO1 AA13488 Zhou (PI) 9/27/01-8/31/05 15%

NIH/NIAAA

“Neuroanatomical adaptation at synaptic level to chronic alcohol”

Investigate how chronic alcohol drinking change the innervation and receptors in the extended amygdala, and examine how would chronic alcohol change the way neurons communicate to each other.

Role: PI

#### Pending

NIH/NIAAA (Zhou) (9/1/04—8/31/08) 15%

“Chronic Alcohol Exposure on Synaptic Adaptation”

Renewal of UO1 AA13488. Investigate how chronic alcohol drinking change on dendritic spines and the receptors in the extended amygdala, and examine how would chronic alcohol change the way neurons communicate to each other.

Role : Principal investigator.





## **Appendix 2**

### **Other Stem Cell Initiatives**

While Indiana could indeed become the first to realize a dedicated, state-funded research center for adult stem cells, state support for stem cell research is certainly being considered and attempted elsewhere. There are 8 states which have legislation that addresses funding for stem cell initiatives: OH, NJ, CA, CT, IL, VA, MA, and IN. Yet few of the 8 states have actually released any money, even in cases where the legislature has voted to allocate funds.

### **Quick Summary**

#### **States with enrolled legislation:**

**California** – established institute with appropriated funding, pending lawsuits

**Connecticut** – established advisory committee (no institute) with appropriated funding

**Illinois** – established institute with appropriated funding

**Indiana** – established task force to assess possibility for center

**Massachusetts** – established advisory council to assess possibility for institute

**New Jersey** – established institute, no money appropriated yet

**Ohio** – established center with appropriated funding

**Virginia** – established research support fund, no money appropriated yet

#### **States considering legislation:**

Florida

Maryland

Missouri

New York

Pennsylvania

Wisconsin

### **Funding Allocated for Embryonic and Adult Stem Cell Research**

#### **California:**

The state of California has made the largest effort to date toward support of stem cell research. With Proposition 71, the California Institute for Reproductive Medicine (CIRM) was established, complete with a governing oversight committee. Through the use of general obligation bonds, the state has allocated up to \$3 billion to fund stem cell research efforts. While no one type of research is targeted for or prevented from support, the emphasis is on embryonic research, with SCNT being among supported efforts. However, certain research groups, such as the Stanford University School of Medicine Institute for Cancer/Stem Cell Biology, have applied to CIRM for funding for researchers using both adult and embryonic stem cells.

As of August 2005, the allocated funds have been stayed by two legal disputes regarding the bond scheme that was slated to generate the need money. The disputes are pending consideration.

(<http://www.smartvoter.org/2004/11/02/ca/state/prop/71/>)

### **Connecticut:**

In May 2005 the Connecticut General Assembly passed SB-934 which provides \$10 million a year for 10 years in funding for embryonic and adult stem cell research, and the bill was signed into law in June 2005. The money will come from the state budget surplus and from a state tobacco settlement. A Stem Cell Research Advisory and Peer Review Committee was established and it is currently being filled. Connecticut law allows therapeutic cloning, but prohibits it for reproductive purposes.

([www.cga.ct.gov/2005/tob/s/2005SB-00934-R01-SB.htm](http://www.cga.ct.gov/2005/tob/s/2005SB-00934-R01-SB.htm))

## **Funding Allocated for Embryonic Stem Cell Research Only**

### **New Jersey:**

New Jersey came close to being the first state to establish a stem cell research institute - with a named director, team of scientists, and plans to recruit more based on the state's January 2004 legalization of embryonic stem cell research. However, the bill signed by former governor McGreevey which established the Center has failed to be given any funding for now. What was initially intended was a \$50 million initiative that would have funded the future institute for 5 years. In June 2005, the legislature voted against a \$150 million sum to build the institute, and a planned public vote on a \$230 million bond issue has been put off. The current governor Codey has committed \$10.5 million from the budget, but the matter of the larger sum has been left to the future.

The state has cited its law as more permissive than federal funding requirements, stating that it "allows life science companies and universities to openly pursue new medical treatments using stem cells."

"The Institute will be one of the first of its kind in the country, and certainly the first to form a real partnership between research universities, a medical school, and private interests."

(<http://www.state.nj.us/treasury/omb/publications/05bib/pdf/bib.pdf>)

### **Illinois:**

In July 2005, the Governor signed an executive order committing state funding to embryonic stem cell research through the Illinois Regenerative Medicine Institute. Initially, \$10 million in grants will be available to researchers working on adult, cord blood, and embryonic stem cells. However, Illinois law prohibits research on embryos from induced abortions and does not allow in vitro creation of embryos for research

purposes only. Originally, the state legislature had considered, and then rejected, a bill allocating \$1 billion over 10 years via bond sale.

(<http://www.illinois.gov/Gov/pdfdocs/execorder2005-6.pdf>)

### **Funding Allocated for Adult Stem Cell Research Only**

#### **Ohio:**

The Center for Stem Cell and Regenerative Medicine began in 2003 with over \$19 million from the state of Ohio. It is composed of researchers from Case Western Reserve University, University Hospitals of Cleveland, The Cleveland Clinic Foundation, Athersys, Inc., and Ohio State University.

“The Mission of the Center is to utilize adult human stem cells and tissue engineering technology to treat human disease.”

“The Vision of the Center is to rapidly translate cutting-edge adult stem cell and tissue engineering laboratory research into the clinic and commercial arenas to replace and repair diseased tissues and organs.”

A similar measure to fund embryonic stem cell research was vetoed in 2005 by governor Taft.

(<http://ora.ra.cwru.edu/stemcellcenter/>)

#### **Virginia:**

The Virginia legislature created a fund to support adult stem cell research in 2005. Money was not appropriated at the time the fund was established. Also, the Virginia senate voted in March 2005 to defeat a bill that would have created an embryonic stem cell research fund.

([www.ncsl.org/programs/health/genetics/esstatefunds.htm](http://www.ncsl.org/programs/health/genetics/esstatefunds.htm))

### **Funding Considered for Embryonic and Adult Stem Cell Research**

#### **Massachusetts:**

In May 2005, the legislature overrode a veto by the governor to pass a law permitting embryonic stem cell research, and establishing a Biomedical Research Advisory Council. The Council will be in connection with the University of Massachusetts Medical School, and is commissioned as a sort of governing board to grant stem cell research

registrations, monitor progress, establish an IRB, and investigate the possibility of creating both a cord blood and placenta bank, as well as an Institute for Regenerative Medicine. Also, the Council will look at what is appropriate state funding for stem cell research. A report is expected in March 2006.

(<http://www.mass.gov/legis/bills/senate/st02/st02039.htm>)

### **Funding Considered for Adult Stem Cell Research Only**

#### **Indiana:**

The General Assembly passed SB-268 in May 2005, which permits embryonic research on stem cell lines consistent with federal funding guidelines. Also, a task force was established to address the possibility of an Adult Stem Cell Research Center, to be in conjunction with Indiana University. No funding for the Center has been appropriated yet.

### **States Looking Into Similar Measures**

**Florida** – ([http://cbs4.com/newslocal/topstoriesmia\\_story\\_216105916.html](http://cbs4.com/newslocal/topstoriesmia_story_216105916.html))

**Maryland** – (<http://mlis.state.md.us/2005rs/bills/sb/sb0751f.pdf>)

**New York** – ([http://grassrootsconnection.com/NY\\_sscn.htm](http://grassrootsconnection.com/NY_sscn.htm))

**Pennsylvania** – (<http://www.thepittsburghchannel.com/news/4806008/detail.html>)

**Wisconsin** – (<http://www.msnbc.msn.com/id/6515491/>)

## Stem cell research legislation:

### **I. OVERVIEW**

The federal policy on sources of embryonic stem cells eligible for federal funding is relative clear in its boundaries, the question of individual state policies is more difficult to identify, especially as a result of the wide spectrum of both the language used and the variable aspects of ESC research which are singled out in existing legislation.

There are currently 31 states possessing specific legislation regarding the permitted and/or restricted uses of embryonic and fetal tissue for scientific research. The range of legislation is from strictly forbidding all embryonic research (South Dakota) to allowing, encouraging, and even specifically funding embryonic research, including that of cloned embryos (California, Connecticut, Massachusetts, New Jersey).

- Many states also contain laws addressing the issue of human tissue purchase/sale.
- Some determine eligible cells by looking to the source of the fetus or embryo, specifically as to whether the either results from an induced abortion.
- Another area with specific provisions is that of the consent required for an aborted fetus or embryo to be used for research purposes.
- Cloning is also addressed by many states: some prohibiting research on cloned embryos, some prohibiting funding for cloning, and some allowing therapeutic while restricting reproductive cloning.

### **II. State by State Evaluation**

The spectrum of state legislation can mostly be simplified into four categories:

1. Specifically permitting research on fetal/embryonic cells
2. Specifically restricting research on fetal/embryonic cells
3. Prohibiting research on aborted or cloned fetuses or embryos
4. Specifically prohibiting research on cloned embryos

In addition, any specific legislation on consent issues or the question of purchase and sale will be indicated as follows:

\* indicates legislation requiring consent

^ indicates legislation prohibiting sale

- ❖ **Specifically permitting research on fetal/embryonic cells**
  - California\*^
  - Connecticut\*^ (before gastrulation)
  - Massachusetts\*^ (less than 14 days old)
  - New Jersey
  
- ❖ **Specifically restricting research on fetal/embryonic cells**
  - Michigan\*
  - Montana
  - North Dakota\*^
  - Ohio^
  - Oklahoma^
  - Pennsylvania\*^
  - South Dakota^
  
- ❖ **Prohibiting research on aborted and/or cloned fetuses or embryos**
  - Arizona
  - Arkansas\*^
  - Florida
  - Illinois\*^
  - Indiana\*^
  - Missouri^
  - Nebraska^
  
- ❖ **Specifically prohibits cloning and/or research on cloned embryos**
  - Iowa^
  - Louisiana
  - Maine^
  - Minnesota^
  - New Hampshire^
  - New Mexico^
  - Rhode Island\*^
  - Utah^
  - Virginia^ (law is ambiguous on the definition of *human being*)
  
- ❖ **Others**
  - Indiana and Kansas follow federal guidelines in determining research eligible for funding
  - Tennessee only prohibits sale of tissue and requires consent
  - Kentucky, Texas, and Wyoming only prohibit sale

Source: <http://www.ncsl.org>