



The University of Western Ontario
 Approved Level 3 Access Approval Form
 Approved: Biohazard Sub-Committee, July 2009

The Biohazard Subcommittee is mandated by the University Biosafety Committee to review requests for access of all personnel working in the Level 3 Facility. Upon approval by the Sub-committee, personnel must be trained by the Biosafety Coordinator (and if applicable ACVS staff) on Level 3 protocols prior to card access being authorized.

1. Name of Personnel Requiring Access (Please Print): Martha Harding
 Name of Personnel Requiring Access (Signature): Martha Harding
 Supervisor (Please Print): Chil-Yong Kang
 Supervisor's Signature: [Signature]

Reason for entry: ^{→ training sessions only.} Research Animal Care Maintenance
 After-Hours Access Required: Yes No

2. Completion of the Following Training:

WHIMIS (renewed every 3 years) Date: Aug 25 '09
 Biosafety Date: Aug 20 '09
 Biosafety Reading:
 Level 3 Biosafety SOP Manual Date: Jan 6 '10
 Laboratory Biosafety Guidelines (2004) Date: Aug 20 '09
 Laboratory Safety and Waste Management Date: Aug 24 '09
 New Employee Orientation Date: _____
 Other(s)**? ACVS animal training Date: mouse training - Aug 26 '08
gas anesthesia Oct 1 '08
Facility (Health Sci) - Nov 11-08

to be completed Jan 13, 2010

3. Entry into the Mandatory Level 3 Medical Surveillance Program:

Date Completed: 24/09/09 Confirmed by: [Signature] RN, COHN

4. Approved by Biohazard Subcommittee: Chair: _____
 Date: _____

5. Completion of Security Check (Complete attached form and submit it to Michael Mico, Manager Campus Police Service):

Date Completed: Nov '09 Confirmed by: [Signature]

6. Completion of Level 3 Training: Date: _____
 Given by: _____

7. Completion of Level 3 Animal Training: Date: _____
 Given by: _____

CURRICULUM VITAE

Name: Martha Jane Harding, DVM, PhD

Born: December 29, 1958; London, Ontario, Canada

Children: Kayla, 19 years and Lara, 16 years

Current Positions: Post-doctoral Research Associate
Laboratory of Dr. Chil-Yong Kang
Department of Microbiology and Immunology
Siebens-Drake Research Institute, Room 129
University of Western Ontario, London, Ontario
Email: mhardin8@uwo.ca

Veterinary Reviewer, Animal Use Sub-Committee
University of Western Ontario, London, Ontario
Email: mhardin8@uwo.ca

Visiting Research Scientist
Department of Immunobiology
Yale University School of Medicine
10 Amistad Street
New Haven, Connecticut 06520
Email: martha.harding@yale.edu

Education

PhD Veterinary Microbiology, College of Veterinary Medicine, University of Minnesota, 1989.
DVM Ontario Veterinary College, University of Guelph, Canada, 1982.

Honors and Recognitions

2005-2008 Research Scholar Award, American Gastroenterology Association
1999 Best Scientific Achievement Award, Pfizer Central Research for the Scientific Paper,
"Duration of Vaccine Immunity in Cats and Dogs". Harding MJ, co-author.
1989 NATO Post-Doctoral Fellowship, Gulbenkian Institute of Science, Oeiras, Portugal.
1984-86 Residency Fellowship in Swine Medicine, University of Minnesota
1982 Merck Veterinary Scholarship, Award for achievement in final year veterinary studies.

Committee Service

October 2009 – present: Veterinary Reviewer, Animal Use Sub-committee, University of Western Ontario.
2001-2008: Veterinary Reviewer and Attending Veterinarian (alternate) Committee Member for the Institutional Animal Care and Use Committee, Yale University.
2003-2005: Committee Member, BL3 Biosafety Committee, Office of Environmental Health and Safety, Yale University

Research Training

August 2008 – present: Post-doctoral Research Associate, Siebens-Drake Research Institute, Department of Microbiology and Immunology, University of Western Ontario in the laboratory of Dr. Chil-Yong Kang. Performing immunological efficacy and safety assessments of candidate hepatitis C virus vaccines in mice.

- September 1995 – July 1997: Post-doctoral research training, James A. Baker Institute for Animal Health, College of Veterinary Medicine, Cornell University in the laboratory of Dr. Colin Parrish, Department of Veterinary Pathobiology. Post-doctoral research training in the molecular biology of canine parvovirus under the supervision of Dr. Colin Parrish, James A. Baker Institute for Animal Health, College of Veterinary Medicine, Cornell University. Studies of canine parvovirus cell receptor, host cell resistance to canine parvovirus infection, early events in the replication cycle of canine parvovirus.
- June 1989 – December 1989 Post-doctoral research training, Gulbenkian Institute of Science, Oeiras, Portugal in the laboratory of Dr. Joao Vasconcelos Costa. Post-doctoral research training in the molecular biology of African swine fever virus under the supervision of Dr. João Vasconcelos Costa, Gulbenkian Institute of Science, Oeiras, Portugal. Studies of African swine fever virus DNA binding proteins.
- September 1984 – April 1989: PhD research training, College of Veterinary Medicine, University of Minnesota in the laboratory of Dr. Thomas Molitor, Department of Veterinary Microbiology and Immunology. PhD research training in the area of virology and immunology under the supervision of Dr. Thomas Molitor, Veterinary Microbiology and Immunology, College of Veterinary Medicine, University of Minnesota. Studies included determination of the porcine parvovirus cell receptor, defining the nature of replicative intermediate forms of DNA in persistent porcine parvovirus infections, porcine parvovirus replication in swine lymphocytes and macrophages.

Employment Experience

- June 2001 - June 2008: Assistant Professor (2001-2007) and Associate Research Scientist (2007 – 2008), Section of Comparative Medicine, Yale University School of Medicine, New Haven, CT. Developing and testing the immune responses in human immune system competent mouse models of human liver pathogens (ie. Hepatitis C Virus) via co-engraftment of human hematopoietic stem cells and human hepatoblasts/hepatocytes in novel strains of immunodeficient mice. Research involved working with mice and cell cultures in a BL2+ facility. Reported to Dr. Robert Jacoby (2001-2006) or Dr. Tamas Horvath (2006-2008), Chairs, Comparative Medicine and Dr. Jordan Pober (research mentor).
- July 2005 – June 2008: IACUC veterinary reviewer. Review veterinary-related issues for IACUC "Modifications" and "Full Applications". Reported to Dr. Jerry Collins, Chair, IACUC.
- July 2002 - July 2005: Yale Veterinary Clinical Service (VCS) / IACUC Veterinary Liaison. Drafted the veterinary consensus for many Policies, Guidelines, Standard Operative Procedures and Best Practices statements (see weblinks below). Served as a consultant to the IACUC for various veterinary issues. Reviewed IACUC "Full Applications" and IACUC "Modifications".
- December 2001 - March 2003: Acting Chief, Veterinary Clinical Service. Reported to Dr. James Macy. Assisted in generation of standard operating procedures regarding animal health care. Supervised managerial and technical veterinary staff. Worked as the primary veterinary clinician for 4-6 months per year, providing veterinary care and consultations for all species of biomedical research animals at Yale.
- February - June 2001: Research Specialist, Department of Pathobiology & Veterinary Science, University of Connecticut, Storrs, CT. Reported to Dr. Antonio Garmendia. Participated in a study monitoring porcine respiratory and reproductive syndrome virus vaccine efficacy and immune responses. Involved implementation of porcine quantitative cytokine assays.
- July 1997 - October 2000: Senior Research Scientist, Animal Health Biologicals Discovery, Pfizer Central Research, Groton, CT. Reported to Drs. Manuel Campos and Robert Yancey. Co-leader for the BVDV and Leptospirosis project teams. Involved with vaccine design and preparation, and co-ordinated model development and vaccine evaluation of novel vaccines in sheep and cattle. Team member for a vaccine project in felines. Involved in development and implementation of clinical, immunologic, virologic, bacteriologic and molecular assays for testing vaccine efficacy.

- January - June 1995: Diagnostic Virologist, Virology Section, Animal Diseases Research Institute, Nepean, Ontario, Canada. Reported to Dr. Robert Heckert. Involved in diagnostic service for foreign animal disease viruses, which involved working in a high security BL-3 facility, supervision of technical staff and revision of protocols. In addition, duties involved participation in diagnostic exercises for the detection of various viruses with a focus of training personnel and comparing utility of conventional and molecular biology methods.
- January 1990 - December 1994: Research Scientist, Virology Section, Animal Diseases Research Institute, Nepean, Ontario, Canada. Reported to Drs. Ahmad Afshar and Gilles Dulac. Involved in the development of diagnostic tests for food animal viruses exotic to Canada using molecular biological approaches. Specifically, projects included polymerase chain reaction (PCR) and nucleotide sequencing methods for the detection of bluetongue, epizootic hemorrhagic disease, hog cholera, pseudorabies, avian influenza and Newcastle disease viruses; production of baculovirus-recombinant antigens for serologic assays for pseudorabies virus. Position entailed working in a high security BL-3 facility.
- September 1982 - August 1984: Veterinarian, Quality Swine Co-operative, Shedden, Ontario, Canada. Reported to Mr. Don McLean and Mr. Jim Hunter. Duties included selection and implementation of computerized bureau record service for member herds, design and implementation of herd health programs for breeding stock herds, herd health consultations in member herds.
- December 1982 - August 1984: Veterinary Coordinator, A and Q Exports, Limited, Embryo Division, Shedden, Ontario, Canada. Reported to Mr. Jim Wilkins. Developed a surgical embryo transfer service company for Canadian swine herds.
- Summers 1976 and 1978: Summer Intern, University of Western Ontario, London, Ontario Canada. Reported to Drs. Fred Possmayer and John Patrick. Worked on studies involving the effect of corticosteroid administration on fetal lung development in guinea-pigs and humans.

Publications

Patents

Senior author on a provisional patent filed August, 1999, Pfizer Central Research, describing pathogenesis of bovine viral diarrhea virus, in collaboration with scientists from Pfizer and the University of Nebraska.

Study Reports

Senior author for 6 Confidential Study reports for United States Department of Agriculture and/or internal Pfizer review, describing bovine viral diarrhea virus and leptospira model development and vaccine trials, 1998-2000.

Manuscripts in Preparation

Harding MJ, Barnaeva E, Bustamante M, Nicholson D, Lepus CM, Rahner C, Lindenbach B, Pober JS, Sjogren MH, Rojkind M. A novel human hepatocyte / human hepatic stellate cell co-culture system that supports long-term hepatocyte gene expression and hepatitis C virus infection *in vitro*. To be submitted to American Journal of Pathology.

Refereed Journals

Harding MJ, Lepus CM, Gibson T, Shepherd BR, Gerber SA, Graham M, Paturzo FX, Rahner C, Madri JA, Bothwell AL, Lindenbach BD, and Pober JS. An implantable vascularized protein gel construct that supports human fetal hepatoblast survival and infection by hepatitis C virus in mice. PLoSone. Submitted, in revision stage.

Choi J-M, Shin J-H, Sohn M-H, Harding MJ, Kim D-Y, Chae W-J, Park S-H, Lee C-G, Lee S-K, Bothwell ALM. Cell permeable Foxp3 protein alleviates autoimmune disease associated with IBD and allergic airway inflammation. Journal of Clinical Investigation. Submitted.

- Lepus C, Gibson T, Krawkova I, Gerber S, Szczepanik M, Hossain J, Bothwell A, Donis RO, Pober JS, Harding MJ. Comparison of Human Fetal Liver, Umbilical Cord Blood, and Adult Blood Hematopoietic Stem Cell Engraftment in NOD-*scid/γc⁺*, Balb/c-*Rag1^{-/-}γc⁺*, and C.B-17-*scid/bg* Immunodeficient Mice. 2009. Human Immunology. Epub Jun 12.
- Brennan MP, Sinusas AJ, Horvath T, Collins JG, Harding MJ. Correlation between body weight changes and postoperative pain in rats treated with meloxicam or buprenorphine. 2009. Lab Animal. 38: 87-93.
- Kirkiles-Smith NC, Harding MJ, Shepherd BR, Fader SA, Yi T, Wang Y, McNiff JM, Lorber MI, Tellides G, Snyder E, Pober JS. Development of a humanized mouse model to study the role of macrophages in allograft injury. 2009. Transplantation. 87:189-97.
- Wittmer CR, Phelps JA, Lepus CM, Saltzman WM, Harding MJ, Van Tassel PR. Multilayer nanofilms as substrates for hepatocellular applications. 2008. Biomaterials. 30:4082-90.
- Wilson JH, Paturzo FX, Johnson L, Mennone A, Boyer JL, Carreiro MP, Hixson DC, Pober JS, Harding MJ. 2006. Rat hepatocyte engraftment in SCID/bg mice using mouse-specific anti-fas antibody. Xenotransplantation. 13:53-62.
- Harding MJ, Cao X, Shams H, Johnson AF, Nelson L, Wheeler DW, Sibert GJ, Vassilev VB, Gil L, Haines D, Campos M, Donis RO. 2002. Role of bovine viral diarrhea virus biotype in the establishment of fetal infections. American Journal of Veterinary Research. 63:1455-63.
- Coyne MJ, Burr JH, Yule TD, Harding MJ, Tresnan DB, McGavin D. 2001. Duration of immunity in dogs after vaccination or naturally acquired infection. Veterinary Record. 149:509-15.
- Coyne MJ, Burr JHH, Tule TD, Harding MJ, Tresnan D, McGavin D. 2001. Duration of immunity in cats after vaccination or naturally acquired infections. Veterinary Record. 149:545-8.
- Prud'homme I, Zhou E-M, Traykova M, Trotter H, Chan M, Afshar A, Harding MJ. 1997. Production of a baculovirus-derived gp50 protein and utilization in a competitive enzyme-linked immunosorbent assay for the serodiagnosis of pseudorabies. Canadian Journal of Veterinary Research. 61:286-291.
- Harding MJ, Prud'homme I, Rola J. 1997. Specificity and nucleotyping studies of a gp50-based polymerase chain reaction test for pseudorabies virus. 1997. Canadian Journal of Veterinary Research. 61:157-160.
- Harding MJ, Prud'homme I, Gradil CM, Heckert RA, Riva J, McLaurin R, Dulac GC, Vydellingum S. 1996. Evaluation of nucleic acid amplification methods for the detection of hog cholera virus. Journal of Veterinary Diagnostic Investigation. 8:414-419.
- Harding MJ, Prud'homme I, Rola J, Dulac GC. 1995. Development of PCR-based tests for the identification of North American isolates of epizootic haemorrhagic disease virus. Canadian Journal of Veterinary Research. 60: 59-64.
- Harding MJ, Prud'homme I, Rola J. 1995. Identification of the major North American bluetongue viruses using nucleic acid amplification techniques. Molecular and Cellular Probes. 9: 223-231.
- Harding MJ, Lutze-Wallace C, Prud'homme I, Zhong X, Rola J. 1994. A reverse transcriptase PCR-based assay for the detection of hog cholera virus. Journal of Clinical Microbiology. 32: 2600-2602.
- Gradil CM, Harding MJ, Lewis K. 1994. The use of the polymerase chain reaction to detect porcine parvovirus associated with swine embryos. American Journal of Veterinary Research. 55: 344-347.
- Harding MJ, Molitor TW. 1992. Production of a monoclonal antibody which recognizes cell surface antigen and inhibits replication of porcine parvovirus. Archives of Virology. 123: 323-333.
- Gradil CM, Molitor TW, Harding MJ, Crabo B. 1990. Excretion of porcine parvovirus through the genital tract of boars: Presence of virus in boar semen. American Journal of Veterinary Research. 51:359-362.
- Harding MJ, Molitor TW. 1988. Porcine parvovirus: Replication in and effect on function of swine peripheral blood lymphocytes and alveolar macrophages. Archives of Virology. 101:105-117.

Book Chapters

- Gradil C, McLaurin R, Prud'homme I, Harding M, Dulac G. 1995. Studies of a hog cholera virus (HCV) contaminant present in porcine kidney cell line IB-RS-2. In: European Society of Veterinary Virology, 3rd edition, M. Schwyzer, M. Ackermann, G. Bertoni et al, eds. Foundation Marcel Merieux, Lyons. pp. 266-271.
- Gradil CM, Harding MJ, Molitor TW, Crabo B. 1991. Boar semen: Transmission and diagnosis of viruses. In: Boar Semen Preservation, 2nd edition, L.A. Johnson and D. Rath, eds. Paul Parey Scientific Publishers, Hamburg. pp. 273-285.
- Molitor TW, Choi CS, Harding MJ, Joo HS. 1986. In utero inoculation to study viral pathogenesis and immunity. In: Swine in Biomedical Research, M.E. Tumbleson, ed. Plenum Publishing Corporation, New York. pp. 1945-1954.

On-line publications

<http://iacuc.yale.edu/policies/postopanalgesia.html>
<http://iacuc.yale.edu/policies/retro-orbital.html>
<http://iacuc.yale.edu/policies/ToeClippingGuidelines.pdf>
<http://iacuc.yale.edu/policies/RodentIdentificationMethods.pdf>
<http://iacuc.yale.edu/policies/RodentAnestheticsVetRecomm.pdf>
<http://iacuc.yale.edu/policies/neuromuscular.html>
<http://iacuc.yale.edu/policies/cylindermaint.html>
<http://iacuc.yale.edu/procedures/opendrop.html>
http://iacuc.yale.edu/procedures/frog_oocyte.html
<http://iacuc.yale.edu/procedures/reaction.html>

Funding

Completed

AGA 07/01/05–06/30/08 35%
Principal Investigator \$65,000/year (07/01/05–06/30/08)
HCV Infection and Pathogenesis Studies in Human Liver Chimeric SCID hu Mice
“Research Scholar Award”

This proposal tested the hypotheses that fresh and cryopreserved fetal, neonatal and adult human liver cells would engraft the liver parenchyma of severely immunodeficient mice, whose endogenous hepatocytes are specifically injured using 3 novel immunological and/or transgenic methods; or would engraft within a subcutaneous vascularized gel; and that cell culture, chimpanzee or human origin isolates of HCV infected these human liver cells maintained either *in vitro* or *in vivo*.

NIH/NHLBI □ 20%
Investigator (Dr. Jordan Pober, Principal Investigator) \$316,912/year (07/01/06–06/30/11)
Endothelial Regulation of Pathogenic T Cells in Graft Atherosclerosis

My contribution to Dr. Pober's R01 project is the development of novel *in vivo* murine models of human immune cell engraftment and function for the purposes of studying the effects of these cells on the allogeneic human artery and skin segments in established graft models in immunodeficient mice.

Yale Liver Center (Harding, Principal Investigator) 09/01/03–08/31/04 \$20,000
Pilot Feasibility Grant

SCID/bg Mouse Models of Hepatitis C Virus Infection

This proposal focused on the optimization of a novel mouse model of rat hepatocyte transplantation in SCID/bg mice using agonistic anti-fas antibody, and supported preliminary studies of human hepatocyte transplantation using similar methodologies.

American Cancer Society (Harding, Principal Investigator) 11/01/02–04/30/04 \$15,000
Development of Human Hepatocyte/SCID Mouse Models for the Study of Hepatitis C Virus Infection.
This proposal developed a novel system of liver injury, using agonistic anti-fas antibody, to support the engraftment of rat hepatocytes in SCID/bg mice.

Recent Teaching Activities

Comparative Medicine Laboratory Animal Medicine Residency Program: Lecturer (Hepatitis, Herpesviruses in Primates, Immunodeficient Rodents, Swine Biology and Medicine, Guinea Pig, Hamster and Rabbit Diseases, IACUC Education), 2005-2007
Quinnipiac Internship Program: Lecturer (Farm Animal Lecture), 2002-2005

Thesis Advisor Activities

Committee Member in the Ph.D. Thesis of Corinne Wittmer, Department of Chemical Engineering, Dr. Paul Van Tassel, Thesis Advisor, October 2006. I was also an active mentor in the design and execution of one portion of Corinne's studies, involving the influence of scaffold coatings on the proliferation and differentiation of rat and human hepatocytes.
Postgraduate Research Trainee Mentor, Advisor to Christin Lepus, June 06 – June 08. Currently an MD/PhD student at Stanford University.

Volunteer Activities

ESL Co-ordinator and tutor for new refugees, Melita House, Guilford CT, 2005-2006.
London Humane Society, London, Ontario, volunteer dog-walker. February 2009 – present.
Habitat for Humanity, London, Ontario, committee member and site volunteer, September 2009 – present.

References

Ruben O. Donis
Chief, Molecular Virology and Vaccines Branch
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