

**CONNIE J. KAPPELER (MARK)**

*Specialties: Developmental and Reproductive Toxicology,  
Reproductive Physiology and Pharmacology*

**Formal Education:**

2007	University of South Dakota Vermillion, SD PhD Basic Biomedical Sciences
2001	University of Nebraska Lincoln, NE BS Biological Sciences Minors: English and Psychology

**Professional Experience:**

	Charles River Laboratories, LLC Ashland, OH
01 Apr 2016 - Present	<u>Position:</u> Staff Toxicologist Developmental and Reproductive Toxicology

Study director for developmental, reproductive and neurotoxicity studies. Responsible for the planning, conduct and successful reporting of assigned GLP studies. Participate in report generation and review process. Prepare technical papers, publications and reports as directed. Develop new capabilities for CRL Ashland. Communicate with sponsors as required.

WIL Research  
Ashland, OH

21 Feb 2012 - 01 Apr 2016	<u>Position:</u> Staff Toxicologist Developmental and Reproductive Toxicology
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Study director for developmental, reproductive and neurotoxicity studies. Responsible for the planning, conduct and successful reporting of assigned GLP studies. Participate in report generation and review process. Prepare technical

papers, publications and reports as directed. Develop new capabilities for WIL Research. Communicate with sponsors as required.

University of Arizona  
Tucson, AZ

July 2008 -  
Feb 2012

Position: Research Associate/Postdoctoral Fellow

Supervised and completed complex experiments in a ovarian toxicology laboratory. Presented work at regional, national, and international conferences. Maintained research funding through a NIEHS-T32 training grant. Mentored graduate, undergraduate, and high school students as they completed their research projects and presented their work at various conferences.

University of South Dakota  
Vermillion, SD

2007 -  
2008

Position: Postdoctoral Fellow

Course director for PHGY 210, includes both lecture and laboratory instruction. Completed research projects on the pathology of endometriosis.

2002 -  
2007

Position: Doctoral Graduate Student

2003-  
2004

Position: Graduate Teaching Assistant

**Articles:**

Dutta, S.; Burks, D.M.; Mark-Kappeler, C.J.; Hoyer, P.B.; Pepling, M.E. The role of steroid hormones in murine oocyte meiotic progression. Submitted to *Biology of Reproduction*.

Dutta, S.; Mark-Kappeler, C.J.; Hoyer, P.B.; Pepling, M.E. The steroid hormone environment during primordial follicle formation in perinatal mouse ovaries. *Biology of Reproduction* **2014**, *91*(3), 1-12.

Eyster, K.M.; Appt, S.; Chalpe, A.; Mark-Kappeler, C.J.; Register, T.C.; Clarkson, T.B. Effects of estradiol on transcriptional profiles in atherosclerotic iliac arteries in ovariectomized cynomolgus macaques. *Menopause* **2014**, *21*(2), 143-52.

Kappeler, C.J.; Hoyer, P.B. 4-vinylcyclohexene diepoxide: a model chemical for ovotoxicity. *Systems Biology in Reproductive Medicine* **2012**, *58(1)*, 57-62.

Eyster, K.M.; Appt, S.; Mark-Kappeler, C.J.; Chalpe, A.; Register, T.C.; Clarkson, T. Gene expression signatures differ with extent of atherosclerosis in monkey iliac artery. *Menopause* **2011**, *18(10)*, 1087-95.

Keating, A.F.; Fernandez, S.M.; Mark-Kappeler, C.J.; Sen, N.; Sipes, I.G.; Hoyer, P.B. Inhibition of PIK3 signaling pathway members by the ovotoxicant 4-vinylcyclohexene diepoxide. *Biology of Reproduction* **2011**, *84(4)*, 743-51.

Mark-Kappeler, C.J.; Martin, D.S.; Eyster, K.M. Estrogens and selective estrogen receptor modulators regulate gene and protein expression in the mesenteric arteries. *Vascular Pharmacology* **2011**, *55(1-3)*, 42-9.

Eyster, K.M.; Hansen, K.A.; Winterton, E.; Klinkova, O.; Drappeau, D.; Mark-Kappeler, C.J. Reciprocal communication between endometrial stromal cells and macrophages. *Reproductive Sciences* **2010**, *17(9)*, 809-22.

Klinkova, O.; Hansen, K.A.; Winterton, E.; Mark, C.J.; Eyster, K.M. Two way communication between endometrial stromal cells and monocytes. *Reproductive Sciences* **2010**, *17(2)*, 125-135.

Mark-Kappeler, C.J.; Sen, N.; Keating, A.F.; Sipes, I.G.; Hoyer, P.B. Distribution and responsiveness of rat anti-Mullerian hormone during ovarian development and VCD-induced ovotoxicity. *Toxicology and Applied Pharmacology* **2010**, *249(1)*, 1-7, (Figure 1E chosen as journal cover art)

Keating, A.F.; Mark, C.J.; Sen, N.; Sipes, I.G.; Hoyer, P.B. Effect of phosphatidylinositol-3 kinase inhibition on ovotoxicity caused by 4-vinylcyclohexene diepoxide and 7, 12-dimethylbenz[a]anthracene in neonatal rat ovaries. *Toxicology and Applied Pharmacology* **2009**, *241*, 127-134.

Martin, D.S.; Redetzke, R.; Vogel, E.; Mark, C.; Eyster, K.M. Effect of ovariectomy on blood pressure and venous tone in female spontaneously hypertensive rats. *Am J Hypertens.* **2008**, *21(9)*, 983-8.

Martin, D.S.; Song, J.; Mark, C.; Eyster, K.M. Understanding the cardiovascular actions of soy isoflavones: potential novel targets for antihypertensive drug development. *Cardiovascular & Hematological Disorders-Drug Targets* **2008**, *8(4)*, 297-312.

Eyster, K.M. Mark, C.J.; Gayle, R.; Martin, D.S. The effects of estrogen and testosterone on gene expression in the rat mesenteric arteries. *Vascul Pharmacol.* **2007**, *47(4)*, 238-48.

Mark, C.J.; Tatchum-Talom, R.; Martin, D.S.; Eyster, K.M. Effects of estrogens and

selective estrogen receptor modulators (SERMs) on vascular reactivity in the perfused mesenteric vascular bed. *Am J Physiol Regul Integr Comp Physiol.* **2007**, 293(5), R1969-75.

Sheth, M.V.; Mark, C.J.; Eyster, K.M. Expression of type 1 and 2A protein phosphatase subunits in the rat corpus luteum across pregnancy. *J Endocrinol.* **2007**, 195(2), 293-9.

### **Invited Review Papers:**

Kappeler, C.J.; Hoyer, P.B. 4-vinylcyclohexene diepoxide: a model chemical for ovotoxicity. *Systems Biology in Reproductive Medicine* **2012**, 58(1), 57-62.

Mark-Kappeler, C.J.; Hoyer, P.B.; Devine P.J. Xenobiotic effects on ovarian pre-antral follicles. *Biology of Reproduction* **2011**, 85(5), 871-83.

### **Abstracts:**

Kappeler, C.J.; Stump, D.G.; Kopp, C.A.; Slotter, E.D.; Coder, P.S. A model to induce superovulation in immature mice. The Teratology Society, **2014**.

Eyster, K.M.; Booze, M.; Drappeau, D.D.; Klinkova, O.; Mark-Kappeler, C.J. Estrogen and selective estrogen receptor modulators regulate gene expression in the liver. *The Endocrine Society*, **2014**.

Dutta, S.; Mark-Kappeler, C.J.; Hoyer, P.B.; Pepling, M. Neonatal mice ovaries secrete estradiol to regulate follicle assembly. *Society for the Study of Reproduction*, **2011**.

Kappeler, C.J.; McKee, L.; Sipes, I.G.; Konhilas, J.; Hoyer, P.B. Inhibition of ovarian Kit autophosphorylation by the ovotoxicant 4-vinylcyclohexene diepoxide. *The Society of Toxicology*, **2011**.

Kappeler, C.J.; Sipes, I.G.; Hoyer, P.B. The critical role of KIT in VCD-induced ovotoxicity. *Society for the Study of Reproduction*, **2011**.

Kappeler, C.J.; Keating, A.F.; Sen, N.; Sipes, I.G.; Hoyer, P.B. Distribution of anti-Müllerian hormone and its receptor in neonatal rat ovaries. *Ovarian Workshop*, **2010**.

Kappeler, C.J.; Keating, A.F.; Sen, N.; Sipes, I.G.; Hoyer, P.B. Distribution of anti-Müllerian hormone and its receptor in neonatal rat ovaries. *The Arizona Physiological Society*, **2010**.

Kappeler, C.J.; Sen, N.; Sipes, I.G.; Hoyer, P.B. Effect of anti-Müllerian hormone on 4-vinylcyclohexene diepoxide-induced ovotoxicity in cultured PND4 rat ovaries. *The Society of Toxicology*, **2010**.

Kappeler, C.J.; Keating, A.F.; Sipes, I.G.; Hoyer, P.B. Role of Kit and PI3K pathway in

7,12-dimethylbenz[a]anthracene-induced ovotoxicity. *The Arizona Physiological Society*, **2009**.

Mark, C.J.; Keating, A.F.; Sipes, I.G.; Hoyer, P.B. Role of Kit and PI3K pathway in 7,12-dimethylbenz[a]anthracene-induced ovotoxicity. *Society for the Study of Reproduction*, **2009**. (included a SSR travel fellowship)

Mark, C.; Tatchum-Talom, R.; Martin, D.; Eyster, K. Effect of estrogens and selective estrogen receptor modulators (SERMs) on the mesenteric arteries. *Centennial Research Symposium*, **2008**.

Mark, C.; Tatchum-Talom, R.; Martin, D.; Eyster, K. Effect of estrogens and selective estrogen receptor modulators (SERMs) on vascular reactivity in the mesenteric arteries. *Sex Steroids and Gender in Cardiovascular-Renal Physiology and Pathophysiology*, **2007**.

Martin, D.; Redetzke, R.; Vogel, E.; Mark, C.; Eyster, K. Gender modulation of venous function in the spontaneously hypertensive rats. *Sex Steroids and Gender in Cardiovascular-Renal Physiology and Pathophysiology*, **2007**.

Mark, C.; Martin, D.; Eyster, K. Effect of estrogen and testosterone on gene expression in the mesenteric arteries. *Society for the Study of Reproduction*, **2006**.

Mark, C.; Martin, D.; Eyster, K. Effect of estrogens on gene expression in the mesenteric artery. *Frontiers in Women's Health Symposium*, **2006**.

Eyster, K.; Mark, C.; Hansen, K. Genomics of Endometriosis. *American Society for Reproductive Medicine*, **2005**.

Mark, C.; Martin, D.; Eyster, K. Estrogens stimulate differential gene expression in the mesenteric arteries. *Dakota Reproductive Symposium*, **2005**.

Mark, C.; Martin, D.; Eyster, K.. Effect of estrogens and SERMs on vascular reactivity in the perfused mesenteric vascular bed *The Gilbert S. Greenwald Symposium on Reproduction*, **2004**.

Mello, A.; Mark, C.; Eyster, K. Stimulation of fatty acid synthase expression in the rat liver by estrogen. *The Gilbert S. Greenwald Symposium on Reproduction*, **2004**.

Mark, C.; Song, J.; Martin, D.; Eyster, K. Oxidative stress in spontaneously hypertensive rats and Wistar-Kyoto rats on a soy vs. casein diet. *Dakota Reproductive Symposium*, **2003**.

### **Presentations:**

“Role of Kit and PI3K pathway in 7,12-dimethylbenz[a]anthracene-induced ovotoxicity.”

Society for the Study of Reproduction Platform Presentation, 2009.

“Effect of Estrogens and Selective Estrogen Receptor Modulators on Vascular Reactivity in the Perfused Mesenteric Vascular Bed.” APS Conference on Sex Steroids and Gender in Cardiovascular-Renal Physiology and Pathophysiology, 2007.

“Effect of Estrogens and SERMs on gene expression in the mesenteric arteries.” University of South Dakota Research Forum, 2006.

“Estrogens Stimulate Differential Gene Expression in the Mesenteric Arteries.” University of South Dakota Research Forum, 2005.

**Book Chapters:**

Eyster, K.M.; Booze, M.; Drappeau, D.D.; Klinkova, O.; Rahman, M.S. and Mark-Kappeler, C.J. Estrogen and selective estrogen receptor modulators regulate differential gene expression in the liver. In *Estradiol: Synthesis, Functions, and Effectiveness*; In press.

Hoyer, P.B.; Mark-Kappeler, C.J. Ovotoxicity in small pre-antral follicles. In *Ovarian Toxicology*, 2<sup>nd</sup> ed.; Hoyer, P. Ed.; CRC Press: Boca Raton, FL, **2014**; pp. 89-115.

**Continuing Education:**

Fetal Alcohol Syndrome Webinar, Presented by Kenneth Jones MD, The Teratology Society, June 17, 2015.

Nonclinical Safety Testing: How well does Toxicology Testing Predict Clinical Outcomes, Presented by Thomas Jones, February 4, 2015.

Recent Developments in the Assessment of Preclinical Seizure Risk, Presented by Joseph Arezzo, February 3, 2015.

Juvenile Animal Studies: Regulatory and Industry Perspectives, Presented by the American College of Toxicology, January 28, 2015.

Implications for Tox/TK When ISR Fails, Presented by the American College of Toxicology, December 3, 2014.

REACH, Alternative Methods, and Tox21: Today and Tomorrow, Presented by the Mid Atlantic Society of Toxicology, May 14, 2014.

Pathology Challenges of Juvenile Toxicology Studies, Presented by George Parker, Society of Toxicologic Pathology, May 9, 2014.

Nonclinical Pediatric Drug Development: Considerations, Study Designs, and Strategies, Presented by the Society of Toxicology, March 23, 2014.

Fundamental Approaches in Immunotoxicity Testing, Presented by American College of Toxicology, February 12, 2014.

Immunotoxicology: Investigations into Undesirable Responses, Presented by Mid-Atlantic Society of Toxicology, May 23, 2013.

Gonadal Development, Function, and Toxicology. Society of Toxicology, 2013.

Immunotoxicology: Investigations into Undesirable Responses. Mid-Atlantic Society of Toxicology, 2013.

Mini-Pig Use in Safety Assessments During Drug Development. Roy Forster, 2013.

Tox 21: Will it succeed?. Dr. Ray Tice, 2013.

Basic Embryology and Developmental Toxicity Testing. Society of Toxicology-Online Course, 2012.

Clinical trial basics. Chris Chengelis, 2012.

Juvenile Toxicology. Mid-Atlantic Society of Toxicology, 2012.

Monitoring molecules in neuroscience: In vivo microdialysis. John Bruno, 2012.

Overview of food safety assessment for biotechnology-derived crops. Monsanto, 2012.

Pollinators and Pesticides: Complementary Components of Sustainable Agriculture. ELSI Specialty Section of SOT, 2012.

Ultrasound evaluation of the effects of drugs on fetoplacental blood flow in cynomolgous monkeys. Bala Krishnan, 2012.

**Honors and Awards:**

Endocrine Society Trainee Travel Award for the Ovarian Workshop, 2010  
Co-chair of the Plenary Lecture: Ovarian Cancer at the Ovarian Workshop, 2010

Society of Toxicology Trainee Travel Award, Reproductive and Developmental Toxicology Section of Society of Toxicology: 2010, 2011

Larry Ewing Memorial Trainee Travel Award: 2006, 2009, 2010, 2011

The American Physiological Society Research Recognition Award, 2007

University of South Dakota Graduate College Research Award: 2004, 2005

Representative, Basic Biomedical Sciences Graduate Student Association, 2004

University of South Dakota Graduate Scholarship: 2001, 2002

Beta Beta Beta Biological Sciences Fraternity: 1999-2001

Phi Sigma Pi National Honor Fraternity: 1999-2001

College of Arts & Sciences Dean's List: 1998, 1999

Exeter Foundation Scholarship: 1997

**Professional Affiliations:**

The Teratology Society, 2012 - present  
Constitutional and Bylaws Committee, 2013-2016  
Abstract Review Committee, 2014

Society of Toxicology, 2008-present  
Reproductive and Developmental Toxicology Section, 2008-present  
Women in Toxicology, 2010-present

Society for the Study of Reproduction, 2004-2013  
Committee on Reproduction and the Environment, 2011-2012  
Trainee Affairs Committee, 2010-2012

Arizona Physiological Society, 2008-2012

American Physiological Society, 2004-2012

**Teaching Experience:**

University of South Dakota, Vermillion, SD  
Undergraduate Course  
PHGY 210 - Human Physiology for Allied Health Professionals  
Lecturer: Endocrine Physiology and Gastrointestinal Physiology: 2003-2004  
Course Director: (both lecture and laboratory instruction): 2007-2008

University of Arizona, Tucson, AZ  
Graduate Course



PCOL573 – Environmental Toxicology Colloquium

Lecturer: “The Ovary and Female Reproductive Toxicology”: April 2010

**Reviewer Service:**

Birth Defects Research Part B: Developmental and Reproductive Toxicology  
Toxicology and Applied Pharmacology  
Reproductive Toxicology