

**BIOMEDICAL & VETERINARY SCIENCES  
GRADUATE PROGRAM**



**ANNOUNCES**

The Doctor of Philosophy Seminar and Examination of

**Michael R. Edwards**

**“Investigations into the role of exogenous  
estrogenic endocrine disrupting chemicals on  
immune dysregulation in autoimmune disease”**

**Wednesday, May 8th, 2019**

**9:00 am**

**VMIA 220**



## Bio



Michael Edwards is a PhD Candidate in the Biomedical and Veterinary Sciences (BMVS) program at Virginia Polytechnic Institute and State University. He earned his B.S. in Biology with a Minor in Chemistry from Longwood University in 2007, and his Doctorate in Veterinary Medicine from Virginia-Maryland College of Veterinary Medicine in 2011. Following his time at Banfield as an Associate Veterinarian, he joined the BMVS program through the T32 Post-DVM Training Program on Animal Models Research for Veterinarians in 2014. His current research explores the effects of exogenous estrogenic endocrine disrupting chemicals on immune responses and kidney disease in mouse models of systemic lupus erythematosus.

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USDA-NIFA

VMCVM Office of Research and Graduate Studies

## Lay Language Abstract

Chemicals that can disrupt the normal effects of hormones are termed endocrine disrupting chemicals (EDCs). Estrogenic EDCs promote or suppress the ability of estrogen receptors to carry out normal functions within the body. Normal immune system functions require a fine balance of inflammatory and anti-inflammatory cellular responses. This delicate balance is a prime target for dysregulation by EDC exposure. Autoimmune diseases, such as systemic lupus erythematosus, are characterized by a loss of immune tolerance to ones' own cells and tissues. There is a lack of knowledge surrounding the immunomodulatory effects of a commonly prescribed EDC, 17 $\alpha$ -ethinyl estradiol, especially as it pertains to autoimmune disease patients. The aim of this dissertation work is to investigate the immunomodulatory effects of exogenous EDC exposure in mouse models of SLE. We found that MRL/lpr mice fed a diet devoid of phytoestrogens had reduced kidney disease and immune-complex deposition and had augmented cytokine response and epigenetics in LPS-stimulated splenic leukocytes compared to mice fed a diet high in isoflavones. We next compared the immunomodulatory effects of chronic pharmacologic dose exposure to 17 $\beta$ -estradiol or EE, and found that while both estrogens have similar effects on innate immune cellular responses, EE has distinct effects on T cell population subsets, cytokine production, gene response and epigenetic alterations in female NZB/WF1 mice. Finally, chronic low-dose oral exposure to EE exacerbated clinical signs of kidney disease and suppressed the normal response of toll-like receptor 9 in

MRL/lpr mice. Overall, we have found that chronic exposure to environmental estrogenic EDCs exacerbates lupus nephritis and alter an already dysregulated immune system in genetically susceptible individuals.

**Publications**

**Edwards, M.**, Dai, R., Heid, B., Cecere, T., Ansar Ahmed, S. Exposure to human relevant doses of 17 $\alpha$ -ethinyl estradiol alters TLR7 and 9 signaling and exacerbates clinical azotemia in female MRL/lpr mice. (In Preparation)

Dai, R.\* , **Edwards, MR.\*** , Heid, B., Ansar Ahmed, S. (2019) 17- $\beta$  estradiol and 17 $\alpha$ -ethinyl estradiol exhibit immunologic and epigenetic regulatory effects in NZB/WF1 female mice. *Endocrinology*. 160(1), 101-118. Doi: 10.1210/en.2018-00824. [\*co-first author].

**Edwards M**, Dai R, Ansar Ahmed S. (2018) Our Environment Shapes Us: The Importance of Environment and Sex Differences in Regulation of Autoantibody Production. *Frontiers in Immunology*. 9(478). doi: 10.3389/fimmu.2018.00478.

Luo XM, **Edwards MR**, Mu Q, Yu Y, Vieson MD, Reilly CM, Ansar Ahmed ,S, Bankole, AA. (2018) Gut microbiota in human systemic lupus erythematosus and a mouse model of lupus. *Applied Environmental Microbiology* 84(4). doi:10.1128/AEM.02288-17

Qinghui Mu; Husen Zhang; Xiaofeng Liao; Kaisen Lin; Hualan Liu; **Michael Edwards**; Ansar Ahmed, S; Ruoxi Yuan; Liwu Li; Thomas Cecere; David Branson; Jay Kirby; Poorna Goswami; Caroline Leeth; Kaitlin Read; Kenneth Oestreich; Miranda Vieson; Christopher Reilly; Xin Luo. (2017). Control of lupus nephritis by changes of gut microbiota. *Microbiome*. July, 5:73.

**Edwards, M.**, Dai, R., Heid, B., Cecere, T., Khan, D., Mu, Q., Cowan, C., Luo, XM., Ansar Ahmed, S. (2017). Commercial rodent diets differentially regulate autoimmune glomerulonephritis, epigenetics, and microbiota in MRL/lpr mice. *International Immunology*. June. 29(6):263-276.

Xin M. Luo, **Michael R. Edwards**, Christopher M. Reilly, Qinghui Mu, S. Ansar Ahmed. "Chapter 8: Diet and Microbes in the Pathogenesis of Lupus." Lupus. Ed. Wahid A. Khan. Rijeka: *Intech*. 2017. <https://www.intechopen.com> Web. (ISBN 978-953-51-3180-9, Print ISBN 978-953-51-3179-3)

## Presentations

## POSTER PRESENTATIONS

Edwards, M., Dai, R., Heid, B., Ansar Ahmed, S. Human-Relevant Dose of 17 $\alpha$ -ethinyl estradiol Exacerbates Glomerulonephritis in the MRL/lpr Mouse. HBCU/MSI Research Summit. Virginia-Maryland College of Veterinary Medicine, Virginia Tech. October, 2018. Blacksburg, VA. USA.

Edwards, M., Dai, R., Heid, B., Ansar Ahmed, S. Human-Relevant Dose of 17 $\alpha$ -ethinyl estradiol Exacerbates Glomerulonephritis in the MRL/lpr Mouse. 34th Annual Graduate Research Symposium, Virginia Polytechnic Institute and State University. March 2018. Blacksburg, VA.

Edwards, M., Dai, R., Heid, B., Ansar Ahmed, S. Human-Relevant Dose of 17 $\alpha$ -ethinyl estradiol Exacerbates Glomerulonephritis in the MRL/lpr Mouse. 29th Annual Research Symposium. Virginia-Maryland College of Veterinary Medicine, Virginia Tech. March 2018. Blacksburg, VA. USA.

Edwards, M., Dai, R., Heid, B., Ansar Ahmed, S. The effect of dietary phytoestrogen on the development of systemic lupus erythematosus in the MRL/lpr mouse. 33rd Annual Graduate Research Symposium, Virginia Polytechnic Institute and State University. March 2017. Blacksburg, VA.

Edwards, M., Dai, R., Heid, B., Ansar Ahmed, S. The effect of dietary phytoestrogen content on the development of systemic lupus erythematosus in the MRL/lpr mouse. 28th Annual Research Symposium. Virginia-Maryland College of Veterinary Medicine, Virginia Tech. March 2017. Blacksburg, VA. USA.

Edwards, M., Dai, R., Heid, B., Ansar Ahmed, S. The effect of dietary phytoestrogen on the development of systemic lupus erythematosus in the MRL/lpr mouse. AAI Annual Conference 2016. American Association of Immunologists. May 2016, Seattle, WA. USA.

Edwards, M., Dai, R., Heid, B., Ansar Ahmed, S. The effect of dietary phytoestrogen on the development of systemic lupus erythematosus in the MRL/lpr mouse. 27th Annual Research Symposium. Virginia-Maryland College of Veterinary Medicine, Virginia Tech. March 2016. Blacksburg, VA. USA.



Edwards, M., Dai, R., Khan, D., Lu, R., Ansar Ahmed, S. The effect of 3 common commercial rodent diets on the development of systemic lupus erythematosus in MRL-lpr mice. 26th Annual Research Symposium. Virginia-Maryland College of Veterinary Medicine, Virginia Tech. March 2015. Blacksburg, VA. USA.

### **ORAL PRESENTATIONS**

Edwards, M., Dai, R., Heid, B., Ansar Ahmed, S. Environmental exposure to 17 $\alpha$ -ethinyl estradiol augments kidney disease and response to infections in female autoimmune-prone MRL/lpr mice. 35th Annual Graduate Research Symposium, Virginia Polytechnic Institute and State University. March 2019. Blacksburg, VA.

Edwards, M., Dai, R., Heid, B., Ansar Ahmed, S. The effect of dietary phytoestrogen on the development of systemic lupus erythematosus in the MRL/lpr mouse. 32nd Annual Graduate Research Symposium, Virginia Polytechnic Institute and State University. March 2016. Blacksburg, VA.

### **Awards and Academic Achievements**

Bronze Award for Oral Presentations, 35<sup>th</sup> Annual GSA Research Symposium, March 27, 2019

### **Examination Graduate Committee**

**Major Advisor/Chair:**

S Ansar Ahmed, B.V.Sc, Ph.D.  
Professor, Immunology  
Associate Dean, Research and Graduate Studies  
Department of Biomedical Sciences and Pathobiology

**Graduate Advising Committee Members:**

Thomas Cecere, DVM, Ph.D., DACVP  
Assistant Professor, Anatomic Pathology  
Department of Biomedical Sciences and Pathobiology

Liwu Li, Ph.D.  
Professor of Public Health  
Department of Medicine

Xin Luo, Ph.D.  
Associate Professor, Immunology  
Department of Biomedical Sciences and Pathobiology

Lijuan Yuan, Ph.D.  
Associate Professor, Virology and Immunology  
Department of Biomedical Sciences and Pathobiology

**External Examiner**

**Divaker Choubey, Ph.D.**

Professor  
Department of Environmental Health  
University of Cincinnati College of Medicine



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