Virginia-Maryland College of Veterinary Medicine

BIOMEDICAL & VETERINARY SCIENCES GRADUATE PROGRAM

ANNOUNCES

The Doctor of Philosophy Seminar and Examination of

Angela M. Ives

"Stress Hormones Modulate Herpes Simplex Virus Infection in Sympathetic, not Sensory, Neurons"

Tuesday, August 8th, 2017
2:00 pm ILSB 1040

Vita/Bio

Angela Ives was raised in Virginia Beach, VA. She graduated from First Colonial High School in 2009. In 2012, she completed an Honors Thesis in Biology at the College of William and Mary with Dr. Paul Heideman on microevolutionary forces in reproductive neuroendocrinological traits. In January 2013, she graduated summa cum laude with a Bachelor's of Science in Biology. Later that year, she was accepted into the dual DVM/PhD program at VMCVM and began working in Dr. Andrea Bertke's neurovirology laboratory as a Biomedical & Veterinary Sciences graduate student. The focus of her PhD work has been the effect of stress hormones on herpes simplex virus infection in primary neurons.

Angela is interested in infectious diseases, neuroscience, and veterinary medicine. She has greatly enjoyed teaching veterinary and undergraduate students, as well as mentoring students in the research lab, and hopes to pursue a career in academia or at a government agency in the field of infectious diseases.

Funded by

NIH National Institute of Allergy and Infectious Diseases
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Publications

Ives AM, Powell-Doherty R, and Bertke AS. (2017). "Epinephrine and corticosterone induce HSV-1 reactivation through their cognate receptors in sympathetic, but not sensory, neurons." (submitted to *Cell, Host & Microbe*).

Ives AM, and Bertke AS. (2017). "Stress hormones epinephrine and corticosterone selectively modulate HSV-1 and HSV-2 productive infection in adult sympathetic, but not sensory, neurons." *J Virol* 91(13): e00582-17.

Yanez AA, Harrell T, Sriranganathan HJ, **Ives AM**, and Bertke AS. (2017). "Neurturin and glial-derived neurotrophic factor selectively maintain HSV1 and HSV2 latency in primary adult sensory neurons." *Pathogens* 6(1).

Lee S, **Ives AM**, and Bertke AS. (2015). "HSV-1 Reactivates from Autonomic Ciliary Ganglia Independently from Sensory Trigeminal Ganglia to Cause Recurrent Ocular Disease." *J Virol* 89(16): 8383-8391.

Presentations

Bertke AS, **Ives AM**, and Yanez AA. Neurotrophic factors and stress hormones selectively regulate herpes simplex virus 1 and 2 (HSV1 and HSV2) infections in peripheral sensory and autonomic neurons. Society of Neuroscience Annual Meeting, Washington D.C., November 2017.

Bertke AS, **Ives AM**, Yanez AA. Neurotrophic factors and stress hormones selectively regulate HSV-1 and HSV-2 infections in peripheral sensory and autonomic neurons. Virginia Viral Pathogenesis Symposium, Norfolk VA, June 2017.

Bertke AS and **Ives AM**. HSV-1 and HSV-2 reactivation in different types of neurons. Colorado Alphaherpesvirus Latency Symposium, Vail CO, May 2017.

Bertke AS, **Ives AM**, Lee S, Yanez AA. Sex, Stress, Neurons and Herpes. University of Kansas, November 2016.

Ives AM and Bertke AS. Epinephrine and Corticosterone Differentially Affect HSV-1 and HSV-2 Productive Infection and Reactivation in Primary Adult Neuronal Cultures. International Herpesvirus Workshop, Madison WI, July 2016. *oral presentation

Lee S, **Ives AM** and Bertke AS. Sympathetic neuronal pathways differentially regulate HSV1 and HSV2 genital infection. International Herpesvirus Workshop, Madison WI, July 2016.

Harrell T, Sriranganathan HJ, Yanez AA, **Ives AM**, and Bertke AS. Neurturin and glial-derived neurotrophic factor, but not nerve growth factor, withdrawal selectively reactivate HSV-1 and HSV-2 from primary adult neuronal cultures. International Herpesvirus Workshop, Madison WI, July 2016.

Powell-Doherty RD, Nelson L, **Ives AM**, and Bertke AS. Latent HSV-1 infection increases AD-related protein plaque formation in primary murine hippocampal neurons. Graduate Research Symposium, Blacksburg VA, March 2016.

Ives AM and Bertke AS. Autonomic and Sensory Neurons Expressing Adrenergic, Glucocorticoid, and Estrogen Receptors Selectively Regulate HSV-1 and HSV-2 Productive Infection. International Herpesvirus Workshop, Boise ID, July 2015.

Ives AM and Bertke AS. Stress Hormone Regulation of Neuron Specificity of Herpes Simplex Virus Type 1 and Type 2 Infection. Society of Neuroscience Annual Meeting, Washington D. C., November 2014.

Bertke AS, Lee S, **Ives AM**. HSV1 and HSV2 in autonomic ganglia. Colorado Alphaherpesvirus Latency Symposium, Vail CO, May 2014.

Ives AM and Bertke AS. Stress hormone regulation of neuron specificity of herpes simplex viruses 1 and 2 reactivation. ILSB Research Symposium, Blacksburg VA, May 2014.

Ives A, Lee S, Kroese L, Brazer L, and Heideman P. Combinatorial Contributions of Heritable Neuroendocrine Variation to Male Infertility. 17th Annual Meeting of the Society for Behavioral Neuroendocrinology, Georgia State University, Atlanta GA, June 2013.

Awards and Academic Achievements

International Herpesvirus Workshop Travel Award for Post-doc and Graduate Trainees (2015, 2016)

Virginia Tech Graduate Research Development Program Award (2015, 2016)

Second Place, ILSB Research Symposium (2014)

Lay Language Abstract

Herpes simplex virus type 1 and 2 (HSV-1 and HSV-2) are major human pathogens, which establish latency in neurons of the peripheral nervous system and reactivate to cause recurrent disease in humans. Physiological stress, which includes the secretion of the stress hormones epinephrine and cortisol, has been associated with increases in severity of clinical signs and increased recurrent disease in humans and animals models of herpetic disease. The mechanism by which physiological stress induces HSV reactivation has been assumed to be through suppression of the immune system. In addition, it has been assumed that sensory neurons harboring latent HSV are the primary source of reactivating virus for recurrent HSV disease. However, my dissertation provides evidence that the stress hormones epinephrine and corticosterone (the animal equivalent of cortisol) can act on peripheral neurons in which the virus is latent, rather than through immune system suppression. In addition, my dissertation provides evidence that the autonomic nervous system, which modulates the physiological stress response, is an important source of reactivating virus to cause recurrent disease. The molecular pathway by which epinephrine and corticosterone induce HSV reactivation in primary adult murine neurons involves specific receptors, transcription factors, and protein kinases that could potentially be targeted in humans for inhibition of HSV reactivation and prevention of herpetic recurrent disease.

Examination Graduate Committee

Major Advisor/Chair:
Andrea S. Bertke, PhD
Assistant Professor of Infectious Diseases
Department of Population Health Sciences

Graduate Advising Committee Members:
Xiang-Jin Meng, MD, MS, PhD
University Distinguished Professor of Molecular Virology
Department of Biomedical Sciences & Pathobiology
Center for Molecular Medicine and Infectious Diseases
Michelle H. Theus, PhD
Assistant Professor Molecular and Cellular Neurobiology
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Associate Professor of Neurobiology
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