

BIOMEDICAL & VETERINARY SCIENCES GRADUATE PROGRAM



ANNOUNCES

The Doctor of Philosophy Seminar
and Examination of

Sheryl Coutermarsh-Ott

**“Investigations into the role of
inflammation in tumorigenesis”**

Friday, November 17, 2017

9:00 am

Phase II, Classroom 125

Vita/Bio



Sheryl grew up in a rural town in northern MD. She graduated from the University of MD-College Park in 2003 with a B.S. in Biology. After a year in lab animal medicine with Charles River Laboratories and three years in small animal practice in Blacksburg, VA, she was accepted into the VA-MD College of Veterinary Medicine in 2007. Here she developed an interest in anatomic pathology and upon graduation in 2011, accepted an anatomic residency position at the University of Georgia. Following her residency completion and board certification, she came back to VMCVM to do a PhD in Dr. Coy Allen's laboratory. Her research here has explored the mechanisms of inflammation in tumorigenesis with a focus on animal models of histiocytic sarcoma and breast cancer. She will continue these investigations in her position as an assistant professor in the Department of Biomedical Sciences and Pathobiology here at VMCVM.

Funded by

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VMCVM Office of Research and Graduate Studies

Lay Language Abstract

The role of inflammation in the development and progression of cancer has been studied for many years. It is well-accepted that chronic inflammation can lead to an environment that is favorable for tumor development. However, more recently it has been shown that being able to escape the immune system and avoid inflammation can also be important in tumor development. The aim of this work was to further investigate these dichotomous roles. In Chapters 1-5 we review and further explore the role of inflammation in a poorly studied tumor called histiocytic sarcoma. Through our studies we have found that a receptor protein present in many cells, NLRX1, is important in the development of chemically-induced HS in mice. Moreover, the development of these tumors is associated with increases in pro-inflammatory and cell growth pathways. Further studies reveal that these pathways are also important to the development of the tumor in dogs. Because HS is rare and poorly studied in humans, we describe the development of an additional mouse model to study HS. This model will help reveal important information about the disease in dogs that can help us study it in humans. Finally, in Chapter 6, we sought to investigate the other potential role of inflammation in decreasing tumorigenesis. In these studies, we used a mouse model of breast cancer to investigate whether or not we could decrease tumorigenesis by increasing the immune system's ability to recognize the tumor.

Publications

Coutermarsh-Ott, S.L.*, Broadway, K.M.*, Scharf, B.E., Allen, I.C. (2017.) Effect of *Salmonella enterica serovar Typhimurium* VNP20009 and VNP20009 with restored chemotaxis on 4T1 mouse mammary carcinoma progression. *Oncotarget* 2017 May 16;8(20):33601-33613. PMID: 28431394.

Coutermarsh-Ott SL*, Doran JT*, Campbell C, Williams TM, Lindsay DS, Allen IC. (2016). Caspase-11 Modulates Inflammation and Attenuates *Toxoplasma gondii* Pathogenesis. *Mediators Inflamm.* 2016;2016:9848263. Epub 2016 Jun 9. PMID: 27378827.

Coutermarsh-Ott S, Simmons A, Capria V, LeRoith T, Wilson JE, Heid B, Philipson CW, Qin Q, Hontecillas-Magarzo R, Bassaganya-Riera J, Ting JP, Dervisis N, Allen IC. NLRX1 suppresses tumorigenesis and attenuates histiocytic sarcoma through the negative regulation of NF-

κ B signaling. *Oncotarget*. 2016 May 31;7(22):33096-110. doi: 10.18632/oncotarget.8861. PMID: 27105514.

Coutermarsh-Ott S*, Eden K*, Allen IC.. Beyond the Inflammasome: Regulatory NLR Modulation of the Host Immune Response Following Virus Exposure. *J Gen Virol*. 2016 Apr;97(4):825-38. Epub 2016 Jan 13. Review. PMID: 26763980.

Brickler, T., Meza, A., **Coutermarsh-Ott, S.**, Hazy, A., Gris, D., Theus, M., Allen, I. (2017.) "Loss of NLRX1 exacerbates neural tissue damage and NF- κ B Signaling following brain injury." *Journal of Immunology*. 2017 Oct 9. PMID: 28993512.

McDaniel, D. K., Jo, A., Ringel, V., **Coutermarsh-Ott, S.**, Rothschild, D.E., Powell, M., Long, T.E., Oestreich, K., Riffle, J.S., Davis, R.M., Allen, I.C. TIPS Pentacene Loaded PEO-PDLLA Core-Shell Nanoparticles have Similar Cellular Uptake Dynamics in M1 and M2 Macrophages and In Corresponding In Vivo Microenvironments. *Nanomedicine: Nanotechnology, Biology, and Medicine*. 2016 Dec 29. PMID: 28040495

Goswami, I., **Coutermarsh-Ott, S.**, Morrison, R.G., Allen, I.C., Davalos, R.V., Verbridge, S.S., Bickford, L.R. (2016). Irreversible electroporation inhibits pro-cancer inflammatory signaling in triple negative breast cancer cells. *Bioelectrochemistry*. 2016 Sep 25;113:42-50. 2016.09.003. PMID: 27693939.

Brickler T, Gresham K, Meza A, **Coutermarsh-Ott S**, Williams TM, Rothschild DE, Allen IC, Theus MH. Nonessential Role for the NLRP1 Inflammasome Complex in a Murine Model of Traumatic Brain Injury. *Mediators Inflamm*. 2016;2016:6373506. Epub 2016 Apr 20. PMID: 27199506.

Williams, Tere M., Rachel A. Leeth, Daniel E. Rothschild, **Sheryl L. Coutermarsh-Ott**, Dylan K. McDaniel, Alysha E. Simmons, Bettina Heid, Thomas E. Cecere, and Irving C. Allen. "The NLRP1 Inflammasome Attenuates Colitis and Colitis-Associated Tumorigenesis." *The Journal of Immunology* 194, no. 7 (2015): 3369-3380. PMID: 25725098.

Williams, Tere M., Rachel A. Leeth, Daniel E. Rothschild, Dylan K. McDaniel, **Sheryl L. Coutermarsh-Ott**, Alysha E. Simmons, Kye H. Kable, Bettina Heid, and Irving C. Allen. "Caspase-11 attenuates gastrointestinal inflammation and experimental colitis pathogenesis."

Presentations

Coutermarsh-Ott, S.L., Eden, K., Dervis, N., Allen, I.C. Inflammatory Signaling Pathways Involved in Canine Histiocytic Sarcoma. Oral presentations at the 28th Annual BMVS Student Research Symposium and 2017 Virginia Tech Graduate Student Assembly Research Symposium, March 2017. Blacksburg, VA

Coutermarsh-Ott, S. and Allen, I.C. Inflammation Exacerbates Pulmonary Tumorigenesis. 27th BMVS Research Symposium and 32nd Graduate Student Assembly Research Symposium. March, 2016. Blacksburg, VA

Coutermarsh-Ott, S., Meza, A., Brickler, T., Ives, A., Bertke, A., Gris, D., Theus, M.*, and Allen, I*. NLRX1 attenuates damage following traumatic brain injury through negatively regulating NF- κ B signaling. 2016 American Association of Immunologist Annual Meeting. Seattle, WA. May 13-17, 2016.

Coutermarsh-Ott, S.L., Eden, K., Dervis, N.G., Allen, I.C. Inflammatory signaling pathways involved in canine histiocytic sarcoma. 2016 American College of Veterinary Pathologists Annual Meeting, New Orleans, LA, December 2016.

Coutermarsh-Ott, S., Simmons, A., Capria, V., LeRoith, T., Heid, B., Washington, C., Dervis, N., Yuzbasiyan-Gurkan, V., Hontecillas-Magarzo, R., Bassaganya-Riera, J., Allen, I.C.** NLRX1 attenuates Tumorigenesis Through the Negative Regulation of AKT and NF- κ B Signaling. American College of Veterinary Pathologists Combined Annual Meeting. Minneapolis, MN. October 17-21, 2015.

Coutermarsh-Ott, S., Simmons, A., Capria, V., LeRoith, T., Heid, B., Washington, C., Dervis, N., Yuzbasiyan-Gurkan, V., Hontecillas-Magarzo, R., Bassaganya-Riera, J., Allen, I.C.** NLRX1 attenuates Tumorigenesis Through the Negative Regulation of AKT and NF- κ B Signaling. Veterinary Cancer Society Annual Conference. Tysons, VA. October 15-17, 2015.

Coutermarsh-Ott, S, Cecere, T, Lanz, O, Barnes, K. Eosinophilic pulmonary granulomatosis in a dog. Oral presentation. 2015 Southeastern Veterinary Pathology Conference, Tifton, GA, May 2015.

Coutermarsh-Ott S. Simmons, A., Capria, V., LeRoith, T., Washington, C., Dervisis, N., Yuzbasiyan-Gurkan, V., Hontecillas-Magarzo, R., Bassaganya-Riera, J., Ting, J., Allen, I.C. NLRX1 attenuates inflammation and tumorigenesis through the negative regulation of AKT and NF- κ B signaling. International Conference: Keystone Conference Z4: Mechanisms of Pro-inflammatory Diseases, Olympic Valley, California, April 19-24, 2015.

Awards and Academic Achievements

2nd place poster award in experimental disease, 65th American College of Veterinary Pathologists Annual Conference (2017)

Outstanding Ph.D. student oral presentation, 28th Annual BMVS Student Research Symposium (2017)

Charles L. Davis Foundation Student Scholarship Award (2015)

Examination Graduate Committee

Major Advisor/Chair:

Irving C. Allen, MS, MBA, PhD

Assistant Professor of Inflammatory Disease
Department of Biomedical Sciences & Pathobiology

Graduate Advising Committee Members:

Nikolaos Dervisis, DVM, PhD

Assistant Professor of Oncology
Department of Small Animal Clinical Sciences

William Huckle, MS, PhD

Associate Professor of Cell Biology and Pharmacology
Department of Small Animal Clinical Sciences

Tanya LeRoith, DVM, Ph.D., Diplomate ACVP

Clinical Associate Professor of Anatomic Pathology
Department of Biomedical Sciences & Pathobiology

Xiang-Jin Meng, MD, MS, Ph.D.

University Distinguished Professor of Molecular Virology
Department of Biomedical Sciences & Pathobiology

External Examiner

Vilma Yuzbasiyan-Gurkan, PhD

Associate Dean for Research and Graduate Studies
Professor

Michigan State University College of Veterinary Medicine