Publications

Possin ME, **Morgan S**, DaSilva D, Tisler C, Pappas T, Roberg K, Anderson E, Evans M, Gangon R, Lemanske R and Gern J. *The relationships between immunoglobulin levels, allergic sensitization and viral respiratory illnesses in early childhood.* Pediatric Allergy Immunology 2010 September; 21(6):990-6

Yamanouchi D, **Morgan S**, Kato K, Lengfeld J, Zhang F and Liu B. *Effects of caspase inhibitor on angiotensin II-induced abdominal aortic aneurysm in apolipoprotein E-deficient mice.* Arteriosclerosis Thrombosis and Vascular Biology 2010 April; 30(4):702-7.

Ellman MB, Kim J, An HS, Kroin JS, Li X, Chen D, Yan D, Buechter DD, Nakayama K, Liu B, **Morgan S**, Im HJ. *The pathophysiological role of the PKCd pathway in the intervertebral disc: In vitro, ex vivo and in vivo studies*. Arthritis Rheum. 2011 Dec 12. Doi: 10.1002/art.34337.

Lengfeld J, Wang Q, Zohlman A, Salvarezza S, **Morgan S**, Ren J, Kato K, Rodriguez-Boulan E, Liu B. *Protein kinase C delta regulates the release of collagen type I from vascular smooth muscle cells via regulation of Cdc42.* Mol Biol Cell. 2012 May; 23(10):1955-63.

Yamanouchi D*, **Morgan S***, Colin Stair, Stephen Seedial, Justin Lengfeld, K. Craig Kent, and Bo Liu. *Accelerated Aneurysmal Dilation Associated with Apoptosis and Inflammation in a Newly Created Modified Calcium Chloride Rodent AAA Model.* Journal of Vascular Surgery 2012 August; 56(2):455-61. **these two authors contributed equally to the manuscript*

Morgan S, Yamanouchi D, Harberg C, Keller M, Burlingham W, Seedial S, Lengfeld J, Liu B. *Protein Kinase C-delta Regulates both Apoptosis and Inflammatory Signaling in Mouse Abdominal Aortic Aneurysm*. Arteriosclerosis Thrombosis and Vascular Biology 2012 October; 32(10):2493-502.

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Stephanie Morgan

Program of the Thesis Defense Seminar for the
Degree of Doctor of Philosophy
in Cellular and Molecular Pathology

"Smooth muscle cell death, macrophage phenotypes, and inflammation in the progression of abdominal aortic aneurysm"

Monday, June 24, 2013
2 pm-4 pm
5001A WIMR

Research conducted in the lab of
Bo Liu, PhD
Department of Surgery

Stephanie Morgan's Thesis Abstract

Smooth muscle cell death, macrophage phenotypes, and inflammation in the progression of abdominal aortic aneurysm

Stephanie E. Morgan
Under the supervision of
Associate Professor Bo Liu, PhD
at the University of Wisconsin-Madison

Apoptosis or programed cell death plays an important role in development, homeostasis, and disease. In most cases, apoptosis removes excessive or damaged cells without eliciting immune responses. However, in certain disease conditions, apoptosis has been shown to stimulate inflammation. The goal of my thesis work is to determine whether and how apoptosis interacts with inflammation in a common and potentially lethal disease called abdominal aortic aneurysm (AAA).

AAA is an age-related vascular disease characterized by progressive aortic dilation. Histologic examination of AAA tissue shows the presence of significant apoptosis, inflammation, and elastin degradation; events which cumulatively result in the weakening of the arterial wall and expansion of arterial circumference. Currently, the only treatment options for aneurysm are surgical or endovascular procedures, and the limitation is due to an incomplete understanding of the biological mechanisms initiating and underlying the disease. The role of apoptosis in aneurysm pathogenesis and progression has not been directly studied. Since vascular smooth muscle cells (VSMCs) are the major source of extracellular matrix (ECM), it was conventionally assumed that apoptosis of VSMCs would contribute to tissue destruction by reducing ECM synthesis. While VSMCs are vital to vascular repair, data generated in our lab suggest another role of apoptosis, i.e. forming an amplification loop with inflammation.

In my thesis work, I explore two related hypotheses. First, chapters 1-4 focus on the idea that ***SMC apoptosis in aneurysmal tissue drives the infiltration of inflammatory cells and the subsequent development of aneurysm.*** In Chapters 1 and 2, we use a pan-caspase inhibitor to prevent apoptosis in three different aneurysm models. In Chapter 3, we show that a modified murine AAA model drives not only an advanced apoptotic and inflammatory response, but also a faster expanding and more severe aneurysm. In Chapter 4, we manipulated apoptosis through Protein Kinase C-delta (PKCδ), a signaling protein our own group has shown to be associated with SMC apoptosis. Once again, we demonstrated the link between SMC apoptosis and pro-inflammatory signaling.

In Chapter 5, I explored mechanism(s) underlying the apoptosis-inflammation interaction. Specifically, we hypothesized that ***the micro-environment within aneurysm tissues causes a shift in monocyte differentiation that results in a reduction in M2 macrophage polarization and diminished M2-mediated clearance of apoptotic cells.*** Furthermore, I tested whether manipulation of macrophage phenotype slows aneurysm progression. In conclusion, the work described here may shed some light on potential therapeutic targets for treatment of human AAA.

Presentations

Poster Presentations:

Experimental Biology; Washington, D.C. April 2011.
Ateriosclerosis, Thrombosis, and Vascular Biology Annual Meeting; Chicago, IL. April 2011.
International Vascular Biology Meeting; Wiesbaden, Germany. June 2012.

Oral Presentation:

March 2013. Title: Cell Death and Inflammation in Abdominal Aortic Aneurysm. Department of Pathology and Laboratory Medicine Seminar Series, Madison, WI.

Honors & Awards

2011, Travel Award to Society of Vascular Surgery Annual Meeting

2011-2013, Predoctoral T32 training grant from UW-Madison Cardiovascular Research Center