Publications


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


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
Apoptosis or programmed 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 microenvironment 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