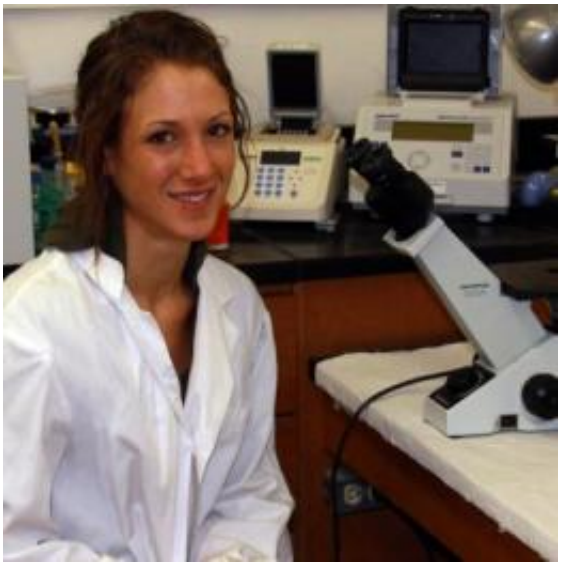
Study says therapeutics for trauma patients may not be effective due to an infection

March 16 2010



Diana Hylton is a K-State senior in microbiology, nutritional sciences and premedicine. She is analyzing how the immune system is involved in damage to the intestines following hemorrhagic shock. Credit: Kansas State University

A Kansas State University study aimed at alleviating intestinal damage in trauma patients digressed to an important finding that could affect medication given to the individuals.

Diana Hylton is a K-State senior in microbiology, nutritional sciences and pre-medicine. She is analyzing how the immune system is involved in damage to the intestines following hemorrhagic shock. While studying

the effects of a complement inhibitor given following hemorrhage, she found that *Helicobacter* infection changes the body's mechanistic response and would therefore affect the therapeutics given to trauma patients.

"The understanding of the different immune processes involved after hemorrhage suggests that the therapeutic potential of some drugs might not be effective on trauma patients with undiagnosed *Helicobacter* infections," Hylton said.

Hylton is working with Sherry Fleming, assistant professor in the Division of Biology. Hylton's project involves studying a mouse model of hemorrhage, which is associated with a sudden rapid loss of a significant amount of blood, and it is common in trauma patients. Hemorrhage causes intestinal damage, and the body responds by activating the complement system.

The complement system is part of the body's natural immune mechanisms to defend against infections. However, uncontrolled and excessive activation can result in inflammatory tissue damage, so trauma victims are given therapeutics to stop the activation. If a therapeutic could stop complement activation briefly, trauma victims would get less tissue damage and improved survival and recovery because the natural immune functions would remain intact.

Hylton has been analyzing changes in the mouse model concerning the intestinal tissue injury and inflammatory response. During the study, the mice became infected with *Helicobacter*, which is a bacteria found in the intestines of animals and humans. The infection often does not show obvious symptoms and therefore is commonly undiagnosed, which causes ulcers as well as liver and colon cancer.

Hylton found that when *Helicobacter* infections are present, they

dramatically change the mechanism causing intestinal injury after hemorrhage. Infected mice did not get intestinal damage from complement activation but rather a different component of the immune system was involved.

"Diana found that mice infected with *Helicobacter* sustain significant intestinal damage in response to hemorrhage, but it is not complement-mediated," Fleming said. "This is important, as many of the therapeutics for hemorrhage are aimed at stopping the complement system, and they do not improve the outcome of infected mice. Thus, trauma patients with undiagnosed infections may require different therapeutics."

Hylton is finishing her central project that involves using a complement inhibitor, administered after hemorrhage, to analyze the changes in the intestinal tissue injury and inflammatory response. The complement inhibitor is delivered locally to the intestinal tissue where complement is activated and binds to certain molecules that have covered the injured cells. This selective binding blocks any further undesirable complement activation that would injure the intestinal tissue.

"I am eager to learn more about how the immune response following hemorrhage is influenced by other immune cells and their secretions," Hylton said. "Cytokines are an exciting area of research because they can have different biological functions in different parts of the body and with different immune responses."

She said initial studies show that IL-12, a small non-antibody molecule that communicates between cells in the body, increases after hemorrhage and is blocked when complement is inhibited. By using mice that are IL-12 deficient, she is studying the pathways and cells involved in IL-12 production after hemorrhage.

Hylton has presented the *Helicobacter* research at the Annual Meeting of

the Society of Leukocyte Biology and at the Annual K-State Research Forum. She presented both the *Helicobacter* and complement inhibitor research at the Kansas Institutional Development Award Network of Biomedical Research Excellence symposium.

Provided by Kansas State University