Researchers discover cause of immune system avoidance of certain pathogens

August 17 2010

A special set of sugars found on some disease-causing pathogens helps those pathogens fight the body's natural defenses as well as vaccines, say two Iowa State University researchers.

This discovery may be a first step in understanding a disease family that includes tuberculosis for which there are currently no good vaccines or cures.

Nicola Pohl, professor of chemistry, and Christine Petersen, assistant professor of veterinary pathology, discovered that a natural coating of sugar interacts with the body's defense cells to dampen its own immune response.

The findings are published in the current online issue of the *Journal of the American Chemical Society*.

Pohl and Petersen began studying persistent pathogens such as tuberculosis and the parasite Leishmania five years ago when they noticed that some types of the parasite can make people sick, while others do not.

"One of the things I was curious about was that pathogenic strains of Leishmania have a different sugar coating on them than nonpathogenic strains," Pohl said.

"We asked the question 'Is it possible that just the sugar coating is

enough to make something pathogenic or nonpathogenic?'" she said.

Leishmania-associated diseases are not usually found in the United States, but have been observed in soldiers returning from the Middle East. The diseases can cause unsightly sores, and can last a period of months, according to Pohl.

The diseases are often fatal to dogs in the United States.

"The problem is, in places like Bangladesh, where people are in a nutritionally compromised state, peoples' immune systems aren't strong enough, and the disease can be fatal," said Pohl.

Normally, when a disease-causing agent enters the body, cells called macrophages engulf and start to destroy the agent.

Leishmania-type diseases are resistant to this process.

To test the theory on the resistance effect of the sugar coating, Pohl and Petersen developed an experiment that required creating small beads measuring one micron in diameter to mimic the pathogens.

One group of beads was then coated with a type of sugar that is similar to that of Leishmania. Another set of beads was coated with a lactose-type sugar that isn't harmful to the cell. A third had no coating.

The beads were then introduced into macrophages.

When the uncoated beads were introduced into the macrophages, the cells noticed the beads and started an immune response, as they should.

When the lactose-covered beads were introduced, they were also recognized and removed.

When the Leishmania-sugar covered beads were introduced, the macrophages took a much longer time to recognize their presence. Then, the immune defense system slowed down or dampened the attacks.

This dampening, Petersen and Pohl showed, is due to an interaction between the sugar on the bead and Toll-like receptor2 (TLR2) within the macrophage.

"There is something inherent about the sugars themselves, and the difference in these sugars, that dampens your normal response to the pathogen," said Pohl.

Pohl said they don't yet know exactly what that interaction is or how it works, but she hopes that this research may lead to more research eventually beating the disease.

"Right now we don't have good therapeutics against Leishmaniasis, and we don't have a vaccine for it, so basically you can't do anything about it," she added.

"The more information we have about this, the more we learn about how to circumvent this to get an effective vaccine," she said.

Petersen credits the partnership with Pohl as one of the key factors in understanding the problem.

Pohl's chemistry background doesn't often lead her to look at whole organisms and Petersen, as a veterinary pathologist, previously didn't look at the chemistry.

"Many of these critical sub-molecular interactions are often glossed over by immunologists and biologists," said Petersen. "But the work Nikki and I just published shows that they can make a much larger difference

in how a pathogen is sensed by the immune system."

Provided by Iowa State University