Protein suggests a new strategy to thwart infection

July 6 2015, by Terry Devitt

The newfound ability of a protein of the intestines and lungs to distinguish between human cells and the cells of bacterial invaders could underpin new strategies to fight infections.

Writing this week (July 6, 2015) in the journal *Nature Structural and Molecular Biology*, a team led by University of Wisconsin-Madison Professor Laura Kiessling describes the knack of a human protein known as intelectin to distinguish between our cells and those of the disease-causing microbes that invade our bodies.

"This has the potential to change the game in terms of how we combat microbes," says Kiessling.

The discovery by Kiessling and several collaborating groups also helps illuminate a previously unrecognized line of defense against microbial invaders. In addition to Kiessling's lab, groups in the labs of UW-Madison bacteriology Professor Katrina Forest, Scripps Research Institute cell and molecular biology Professor James Paulson, and Emory University biochemistry Professor Richard Cummings contributed to the study.

Intelectin is not new to science, Kiessling notes, but its ability to selectively identify many different kinds of pathogens and distinguish those cells from human cells was unknown.

"The protein is upregulated with infection," explains Kiessling, "and

while no one has yet shown that it is an antimicrobial protein, there are multiple lines of evidence that suggest it is."

TheWisconsin group established that intelectin has all the properties needed to function in the immune system's surveillance complex. That makes sense, Kiessling explains, as the protein is found mostly in the cells in the intestine and respiratory system, the places most likely to be entry points for microbial pathogens.

Intelectin performs its surveillance role through its ability to selectively recognize the carbohydrate molecules that reside on the surface of cells. Both mammalian cells and microbial cells have carbohydrates known as glycans on their cell surfaces. However, the chemical structures of the glycan molecules vary, and the molecules that decorate the surface of human cells are markedly different from those on microbial cells.

By exposing human intelectin to arrays of both human and microbial glycanS, Kiessling and her colleagues found that intelectin could recognize different kinds of microbes as well as distinguish between microbial and mammalian glycans.

The role of intelectin in immune response, Kiessling believes, is likely ancient. The same kinds of proteins are found in many different kinds of animals, including sheep, mice frogs, eels, fish and even sea squirts, suggesting it has been conserved through evolutionary history.

The glycans to which intelectin attaches, however, can be vastly different. In humans, for example, less than 35 chemical building blocks are used to make the cell surface molecules. In bacteria, nature deploys more than 700 chemical building blocks to make glycans. This immense increase in diversity can make accurate detection difficult.

"Human intelectin just recognizes a small portion of the glycan, a shared

feature like a handle," explains Kiessling. "Then it can recognize when the handles appear, even when different types of bacteria make different glycans."

The larger insight from the study could aid in the design of the next generation of antibiotics, which are urgently needed as many pathogens have become resistant to the antibiotics now most commonly used to treat infection.

More information: Recognition of microbial glycans by human intelectin-1, DOI: 10.1038/nsmb.3053

Provided by University of Wisconsin-Madison