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Blood type A may predispose to some rotavirus infections

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Whether you become infected by some strains of rotavirus may depend on your blood type.

Some strains of rotavirus find their way into the cells of the gastrointestinal tract by recognizing antigens associated with the type A blood group, a finding that represents a new paradigm in understanding how this gut pathogen infects humans, said Baylor College of Medicine researchers in an online report in the journal *Nature*.

Rotavirus is a major intestinal pathogen that is the leading cause of severe dehydration and diarrhea in infants around the world. An estimated 500,000 people worldwide die from the infection annually.

The structure of a key part of a strain of the virus known as P[14] provides a clue to how the virus infects human cells, said Dr. B. V. Venkataram Prasad, professor of biochemistry and molecular biology at BCM and the report's corresponding author. In strains of rotavirus that infect animals, the top of a spike on the virus attaches to the cell via a glycan (one of many sugars linked together to form complex branched-chain structures) with a terminal molecule of sialic acid. The same did not appear to be true of virus strains that infect humans, and scientists believed the human rotavirus strains were bound to glycans with an internal sialic acid molecule, but they did not know how this occurs.

"We wondered how this genotype of rotavirus recognized a cellular glycan," said Prasad. "With colleagues at Emory (University School of

Medicine), we did a glycan array analysis to see which glycans interacted with the top of the virus spike (called VP8*)."

The only type of glycan that interacted with VP8* was type A histo-blood group antigen, he said.

"That was surprising," he said. "We thought it had to be a glycan with sialic acid."

The histo-blood group antigen A does not have sialic acid.

However, when Dr. Liya Hu, a post-doctoral researcher in Prasad's laboratory, determined the structure of the VP8* domain, she found that the type A glycan bound to the rotavirus spike protein at the same place as the sialic acid would have in an animal rotavirus. Histo-blood group antigens are known to promote binding of norovirus and Helicobacter pylori cells to intestinal cells, but this had never been demonstrated in rotavirus.

Hu's structural study, using crystallography, showed subtle changes in the structure of the VP8* domain of the virus that allowed it to use the histo-blood group antigen A as a receptor.

In collaboration with the laboratory of Dr. Mary Estes, professor of molecular virology and microbiology at BCM, Prasad and his colleagues found that laboratory cells modified to express the histo-blood group antigen A were easily infected by this rotavirus strain. Cells that lacked this antigen were not easily infected.

An antibody to the histo-blood group antigen A blocked infection by the virus into human intestinal cells in culture.

"No one expected this," said Prasad. "Is there an emerging theme here

with these intestinal pathogens? Do other viruses use these blood group antigens as a door to enter the cell?"

Further studies identified a second rotavirus strain P[9] that uses the histo-blood group antigen as a receptor, he said.

"The question now is do different strains use other histo-blood group antigens in this way?" he said.

Estes said, "These studies are significant because they provide a novel mechanism of transmission for a rotavirus strain that jumps from ungulates (such as horses, zebras, pigs, sheep) into humans."

The authors found humans infected with the P[14] strain had type A blood, but more studies are needed to confirm the connection.

Larger populations of infected individuals need to be studied to determine if there is a clear association of these virus strains using histo-blood group antigens as a receptor," they said.

This finding raises questions about why humans developed different blood groups, Prasad said. It may be an evolutionary change that occurred after the pathogen first invaded human cells.

Provided by Baylor College of Medicine

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