

Integrins as receptors give insight into rotavirus and diarrhea

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Eleven years ago, Dr. Mary Estes of Baylor College of Medicine and her colleagues discovered the first viral enterotoxin, rotavirus NSP4, a toxic protein that affects the intestines, causing diarrhea.

The next step was to find the cellular receptor on intestinal cells through which the enterotoxin interacts to cause diarrhea.

"We knew that identifying the receptor might not be straightforward," said the professor of molecular virology and microbiology at BCM. In a report online in the *Proceedings of the National Academy of Sciences*, Estes and her colleagues describe two receptors for the enterotoxin, both of them integrins.

The two, integrin alpha1 beta1 and integrin alpha2 beta1, are members of a class of molecules that are involved in attaching cells to other cells and to the extracellular matrix (a part of tissue that is not part of any cell). Integrins also are involved in transforming or translating cell signals.

In looking for the receptor, Estes and her colleagues also learned more about the enterotoxin itself.

"It's a new ligand for binding to integrins," she said. "It begins to give us an understanding of how the enterotoxin works in the intestine. Two different domains of the enterotoxin are involved in this interaction. One domain is for binding and the other domain is for signaling through the

receptor."

She said she hopes to study the signaling aspect of the enterotoxin more closely because it could hold the clue to the mechanism of induction of diarrheal disease.

"There may be ways to block the interaction between the enterotoxin and the receptor to treat diarrheal disease," said Estes, who is also director of the Texas Medical Center Digestive Diseases Center.

Rotavirus is one of the most common causes of diarrhea, resulting in approximately 3 million cases of diarrhea and 55,000 hospitalizations for diarrhea and dehydration in children under the age of 5 each year in the United States alone. Worldwide, it causes nearly half a million deaths each year. Finding out how rotavirus causes diarrhea and looking for ways to block it is a major aim of Estes' research.

Source: Baylor College of Medicine

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