MedicalXpress

Researchers identify novel mechanism that helps stomach bug cause illness

July 29 2013

A seafood contaminant that thrives in brackish water during the summer works like a spy to infiltrate cells and quickly open communication channels to sicken the host, researchers at UT Southwestern Medical Center report.

Vibrio parahaemolyticus bacteria, which cause gastroenteritis, inject proteins called effectors into host cells. One of those effectors, VopQ, almost immediately starts to disrupt the important process of autophagy via a novel channel-forming mechanism, the scientists report in the investigation available online at the *Proceedings of the National Academy of Sciences*. Autophagy is the cellular housekeeping mechanism used to recycle nutrients in cells as well as to fight off pathogens. The term autophagy comes from the Greek words for self and eating. During the process, nutrients are recycled by the lysosome, an internal organelle, to produce metabolites that can be used by the cell.

"Our study identifies a bacterial effector that creates gated ion channels and reveals a novel mechanism that may regulate autophagy," said Dr. Kim Orth, professor of molecular biology and biochemistry. She is a corresponding author on the published study. The first author is Anju Sreelatha, a graduate student in Dr. Orth's laboratory.

"Disruptions of autophagic pathways are implicated in many human diseases, including neurodegenerative disease, liver disease, some cancers, and cardiomyopathy (heart muscle disease)," Ms. Sreelatha said.

She explained that ion channels are pores in the membranes of cells or of organelles within cells that allow regulated passage of small molecules or ions across membranes. Gated channels have a mechanism that opens and closes them, making these proteins potential targets for drug development.

"The identification of a channel that opens and closes and thereby affects autophagy may give us a handle by which to modulate this important process," she said, adding that the researchers found that VopQ's channel activity turned off autophagy.

"During infection, VopQ is injected into the host cell where the protein binds to a lysosomal membrane protein and forms small pores, all within minutes of infection. The resulting complex of proteins causes ions to leak and the lysosomes to de-acidify. Lacking acidification, lysosomes cannot degrade the unneeded cellular components and autophagy is disrupted," Ms. Sreelatha said.

Dr. Orth said "Bacterial pathogens have evolved a number of ways to target and manipulate host cell signaling; the ability of VopQ to form a gated ion channel and to inhibit autophagy represents a novel mechanism."

Further characterization of the mechanism by which VopQ sabotages cells to disrupt autophagy may lead to a better understanding of host-pathogen interactions as well as advance our understanding of the pathway, eventually leading to new treatments for diseases in which autophagy has gone awry, they noted.

Provided by UT Southwestern Medical Center