Researchers uncover attack mechanism of illness-inducing bacterium

August 18 2008

An infectious ocean-dwelling bacterium found in oysters and other shellfish kills its host's cells by causing them to burst, providing the invader with a nutrient-rich meal, researchers at UT Southwestern Medical Center have found.

The bacterium, a relative of the one that causes cholera, co-opts and makes fatal a normal cell process that starving or stressed organisms use to disassemble and recycle expendable proteins into more vital metabolites.

Called *Vibrio parahaemolyticus*, or V para for short, the bacterium is already a major cause of human illness and economic loss in Asia. It is dangerous primarily to people with liver disease or suppressed immune systems, although it can be killed by fully cooking shellfish, according to the U.S. Centers for Disease Control and Prevention.

It caused major disease outbreaks in the northwest and northeast U.S. in the late 1990s and killed two people after Hurricane Katrina when tainted seawater entered open wounds, according to the CDC and the U.S. Food and Drug Administration.

"This pathogen has spread to all the oceans of the world, and is resistant to many antibiotics," said Dr. Kim Orth, associate professor of molecular biology and senior author of a study appearing online this week and in an upcoming issue of the *Proceedings of the National Academy of Sciences.*

Dr. Orth said she became interested in V para after its DNA was sequenced by Japanese researchers. She saw similarities between some of V para's genes and those encoded by an unrelated bacterium that causes plague, which she also studies.

V para was already known to kill host cells but the molecular mechanisms were unclear, Dr. Orth said. However, the new study shows that V para physically contacts host cells and then injects molecules to trigger the protein breakdown process.

Normally, this protein breakdown mechanism, called autophagy (pronounced "aw-TAH-fah-gee") or "self-eating," is tightly controlled by the cells.

In the study, the researchers infected cultured human cells with V para and found that the cells very quickly showed signs of autophagy, such as forming distinctive small compartments that collect and transport proteins for disassembly.

The cells also became rounded, probably from a collapse of their internal framework, and their outer membranes began leaking, the researchers found. The cells died within three hours.

The researchers hypothesized that the invading V para scavenged nutrients from the dying cells to support their own proliferation.

"No one has seen such a rapid triggering of autophagy before," said Dr. Orth.

"Treating the human cells with an autophagy inhibitor halted the protein breakdown process but did not save the cells, because V para uses other pathways by which to kill cells," she said. "However, because it can kill by several routes, it's important to understand all of them."

In addition, because of rising ocean temperatures, the brackish conditions that favor V para growth extend farther north along the U.S. coasts.

"We've received a wake-up call that this is important environmentally, and we want to understand at the molecular level how this pathogen infects, kills and persists," Dr. Orth said. "There are people getting sick from this emerging pathogen in the United States, yet there is no major effort to understand its pathology.

"There are many ways to kill a cell, and we've discovered yet another one. The bacterium hijacks activities from us and deregulates them. It's like a bulldozer."

Although less dangerous than cholera, V para causes similar symptoms: diarrhea, nausea, vomiting and fever. In general, people recover in about three days, needing only rest and fluids, according to the CDC. One of the fatalities from the Hurricane Katrina aftermath had human immunodeficiency virus; details on the other case were not available.

Source: UT Southwestern Medical Center