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RESEARCH NEWS

AUGUST 21, 2005

Hide and Seek:Researchers Discover a New Way for Infectious Bacteria to Enter Cells

French scientists have learned how *Listeria monocytogenes* , which causes a major food-borne illness, commandeers cellular transport machinery to invade cells and hide from the body's immune system. They believe that other infectious organisms may use the same mechanism.

The *Listeria* bacterium, found in soil and water, can be transmitted to humans via undercooked and unpasteurized food, causing flu-like symptoms or gastrointestinal distress. For individuals with weakened immune systems, listeriosis can be fatal, and infections during pregnancy can lead to miscarriage, stillbirth, premature delivery, or infection of the newborn.

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> **— Pascale F. Cossart**

The research was conducted by Pascale Cossart, a Howard Hughes Medical Institute international research scholar, and her colleague Esteban Veiga at the Institut Pasteur in Paris, and will be published in the August 21, 2005, issue of *Nature Cell Biology* . Cossart and Veiga detailed how *Listeria* invades cells by activating cellular machinery that transports viruses, small molecules, and proteins. Once it has safely entered a cell, the microbe can replicate and continue the process of infection.

The body usually deals with bacteria and other large, foreign microbes through a process called phagocytosis. Specialized cells engulf the invading microbe and destroy it. Scientists long believed that cells use a second process, called endocytosis, to deal with smaller molecules or viruses. In endocytsosis, a cell's outer membrane pinches inward around the target to form a pocket that's brought inside the cell, creating a structure called a vesicle.

“Phagocytosis and endocytosis may, in fact, be more similar than past research suggests. This is a totally new concept,” Cossart says.

Cossart's lab had observed that *Listeria* - which is 20 times the size of the largest particle scientists believed a cell could take in by endocytosis - could invade non-phagocytic cells. Other labs had made similar observations with other bacteria. Cossart and Veiga investigated the underlying machinery behind this uncommon invasion strategy, which they knew depended on an interaction between a protein on the surface of the bacteria, known as InlB, and a protein called Met on the surface of the cell it was invading.

They discovered that when InlB interacts with Met, the cell responds by adding a chemical tag to Met that flags it for protein recycling or degradation. Since Met is on the outside surface of the cell and the recycling and degradation machineries are inside, the cell must bring Met inside through endocytosis in order to dispose of it. As the cell creates the vesicle that will transport tagged Met, *Listeria* stows away and invades the cell.

By manipulating the gene expression of the cells *Listeria* was invading, the researchers showed that specific molecules known to be involved in endocytosis were essential for successful invasion by *Listeria* . Similarly, they found that an enzyme that tags proteins for recycling was also required.

Listeria's use of receptor-mediated endocytosis to infect hosts, according to Cossart, suggests that other bacteria may exploit the same mechanism to gain entry into non-phagocytic cells. “This mechanism of cell entry may be used by several different kinds of bacteria, which is a major deviation from the belief that endocytosis is strictly for importing small molecules into cells,” she says.