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Listeria Hijacks a New Protein

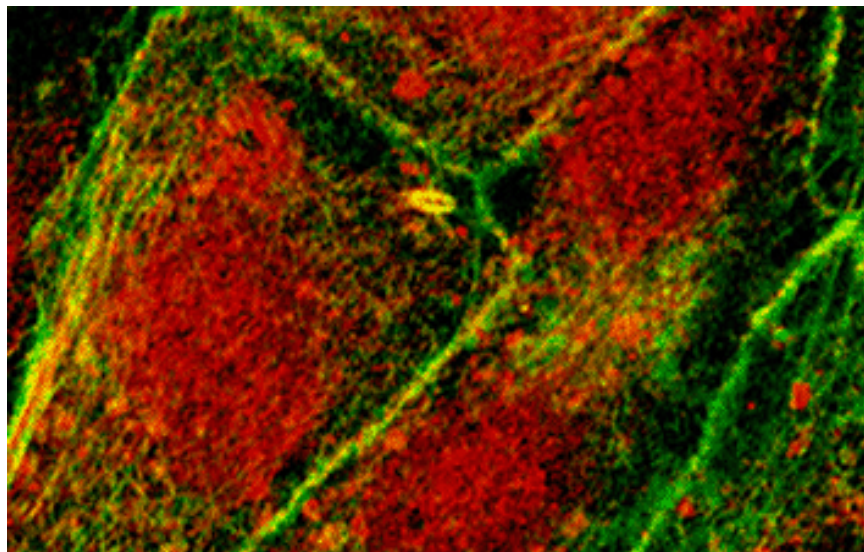


Image Title: Listeria entering epithelial cells. Actin is labeled in red and a protein of the junctional complex myosinVII is labeled in green. At the site of bacterial entry, both actin and myosinVII are found. - Sandra Sousa and Pascale Cossart, Pasteur Institute

Scientists taking a close look at how a dangerous food-borne bacterium invades the gut have identified a new culprit—a molecule that normally helps hold the intestinal lining and other sheets of epithelial cells together.

The French researchers report their findings in the October issue of the journal *Nature Cell Biology*.

“*Listeria*, like many pathogens, exploits molecules used by the cell for other functions,” said senior author Pascale Cossart, a Howard Hughes Medical Institute international research scholar at the Institut Pasteur in Paris. “The new protein plays a key role in the formation of adherens junctions of epithelial cells, and *Listeria* uses it for its own infectious process.”

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Listeria monocytogenes, often found in soft cheeses and processed meats, causes an infection that can spread from the intestine to the liver and spleen and ultimately to the brain and placenta. The infection from *Listeria* is fatal in an estimated 20 to 30 percent of cases and can kill fetuses in pregnant women.

The study, led by Cossart's postdoctoral fellow and colleague Sandra Sousa, reveals new details of *Listeria*'s invasion strategy. It also provides new insights into how the epithelial cells that line the body and its organs stick together.

Epithelial cells cover the surfaces of skin, lungs, mouth, gastrointestinal tract, reproductive and urinary tracts, and various glands. The cells use sticky molecules called E-cadherins to adhere to each other. Inside epithelial cells, E-cadherin molecules are anchored to the cell cytoskeleton, which controls cell shape and plasticity.

About 10 years ago, Cossart's group discovered a protein on the surface of *Listeria* that can attach itself to E-cadherin, allowing the bacterium to invade human epithelial cells. The protein triggers the dynamic cytoskeleton within the cell to surround and enclose the bacterium. Once enfolded, the bacterium enters the cell. Inside the cell, *Listeria* is protected from antibacterial products and then spreads surreptitiously to nearby cells.

Actin, the protein that makes up the cytoskeleton, can form long filaments that grow in one direction and networks of filaments. Many proteins control the formation or disaggregation of these filaments. "*Listeria* is famous because it exploits actin and forms actin tails which help the bacterium to move inside cells," Cossart explained.

As she followed the trail of *Listeria* into the cell, Cossart and other scientists began to suspect that the junctions were behaving in a more complex manner than originally thought. Inside the epithelial cell, the tail of E-cadherin binds to a protein called α -catenin, which recruits other proteins that spur assembly and disassembly of actin filaments and is absolutely critical for strong adherence between epithelial cells.

The researchers searched hundreds of molecules for potential partners of α -catenin and turned up a new protein known only by its sequence in the human genome database: ARHGAP10. To study that protein's role, they used human cell cultures.

Using colorfully labeled antibodies to light up the new protein under their microscopes, they found that it was present where *Listeria* entered cells and also present at adherens junctions between epithelial cells. When they blocked expression of the new protein with small interfering RNA, a chemical cousin of DNA, *Listeria* could not enter the cell, and epithelial cells did not recruit α -catenin at their junctions.

Meanwhile, another group of French researchers identified the same protein, ARHGAP10, as a partner with two other molecules—Arf1 and Arf6—involved in both actin dynamics deep within the cell and the turnover of adherens junctions.

The findings, Cossart said, “are further evidence that *Listeria* is particularly effective at exploiting the cells' own components to facilitate invasion. The bacterium will be a useful tool for studying the complex cellular events that occur at cell-to-cell junctions,” she added.