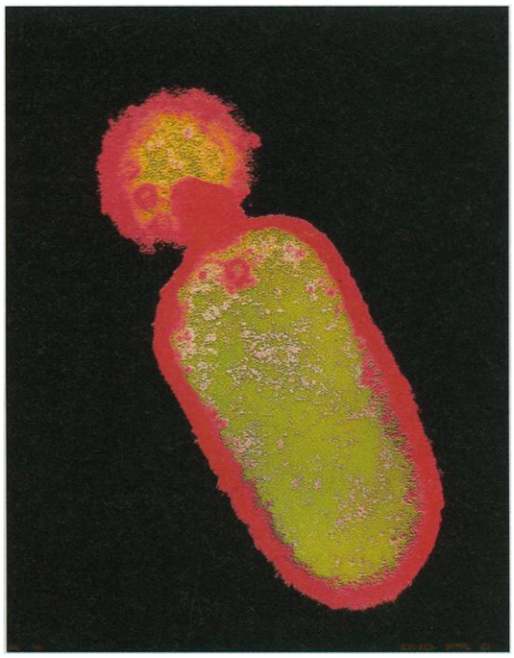
Enter *Listeria*, Unruffled

For many pathogens, the inside of mammalian cells represents an ideal protected niche, away from circulating antibodies and other host defenses. Understanding how microbes trigger their own uptake into nonphagocytic cells, a process known as induced phagocytosis, is at the top of the agenda of the emerging field of cellular microbiology (*1*). Work on a trio of Gram-negative bacteria—*Yersinia*, *Salmonella*, and *Shigella*—has blazed the trail, but a recent paper from the Pasteur Institute in *Cell* (*2*) provides the first details of how a Gram-positive bacterium, *Listeria monocytogenes*, is taken up.

The protein on *Listeria*'s surface that interacts with mammalian cells was described some years ago (*3*): It is internalin, an 80-kilodalton protein that is a member of the growing family of LRRs (leucine-rich repeats) proteins. The new work shows that the receptor for internalin on the surface of epithelial cells is E-cadherin. That the two proteins interact was revealed by affinity chromatography: Amino-terminal sequencing identified the two epithelial cell products retained on an internalin column as E-cadherin and its proteolytic fragment. The authors emphasize the significance of the interaction by testing the ability of *Listeria* strains (with and without internalin) to invade panels of fibroblastic cell lines expressing different cadherins. Invasion was prevented when the fibroblasts expressed N-cadherin instead of E-cadherin. Thus, the internalin–E-cadherin interaction mediates both specific binding and entry of the bacterium, a finding supported by the blockade of invasion by antibodies to E-cadherin.



Listeria monocytogenes. Electron micrograph of a *Listeria* bacteria with daughter cell at top left; 54,000× [Photo by K. Lounatmaa, Photo Researchers Inc.]

E-cadherin is a member of the cadherin family of cell adhesion molecules, which mediate cell-cell adhesion through homotypic interactions of their extracellular domains. E-cadherin is expressed mainly on epithelial cells and participates in cell sorting during development and in the maintenance of adult tissue architecture. Cadherins are connected to the actin cytoskeleton by their cytoplasmic domains through interactions with catenins.

The new work from Mengaud *et al.* (*2*) does not prove that signaling through E-cadherin mediates the induced-phagocytosis of *Listeria*, but the actin polymerization that occurs at the site of entry is a tantalizing hint in this direction. The amount of F-actin accumulation is modest, considerably lower than that found with the entry of *Salmonella* and *Shigella*, which is accompanied by dramatic localized membrane ruffling. For *Listeria* there is no membrane ruffling, and the process is similar, morphologically, to the entry of *Yersinia* mediated by the cell-surface protein invasin (*4*). Clearly, the haven of the mammalian cell is so desirable that bacteria have developed multiple strategies of entry.

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cial evolution, perhaps for as yet undiscovered communicative functions. Is the biosynthetic machinery of the queen more intricate? Plettner *et al.* show that 9-ODA, the principal queen mandibular acid, is only produced after a third reaction in which 9-HDA is oxidized; in workers the oxidation of 10-HDA yields diacid (C10:1DA), a minor component, at least quantitatively (*7*). Queens also have about 10 times more mandibular acid than do workers. Despite these distinctions, the biosynthesis of mandibular acids in the two castes reveals intriguing overlap. Plettner and colleagues show that very young virgin queens can oxidize 10-HDA to the diacid like workers, and previously they found 9-HDA in workers (*7*). But neither workers nor young virgin queens oxidize 9-HDA to 9-ODA, whereas older virgins and mated queens can. "False queens" are an exception; these workers, which sometimes develop in queenless, broodless, colonies and lay male eggs, have queenlike mandibular gland secretions, complete with a lot of 9-ODA (*7*, *8*). Caste differences in mandibular acid biosynthesis thus appear to be sensitive to both intrinsic and extrinsic factors. Further exploration of how these factors influence mandibular gland biosynthesis may lead to new insights into the evolution of the worker and queen castes, a central question in sociobiology. Another fertile line of investigation now possible is to identify the enzymes involved in mandibular gland pheromone biosynthesis, and their genes, and study their regulation as a function of age, mating status, and social condition. No one has yet reported the cloning of a pheromone biosynthesis gene. There is no doubt that honeybee queen mandibular pheromone, already an exemplar, will continue to be used as a chemical beacon in both sociobiology and chemical ecology.

References

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