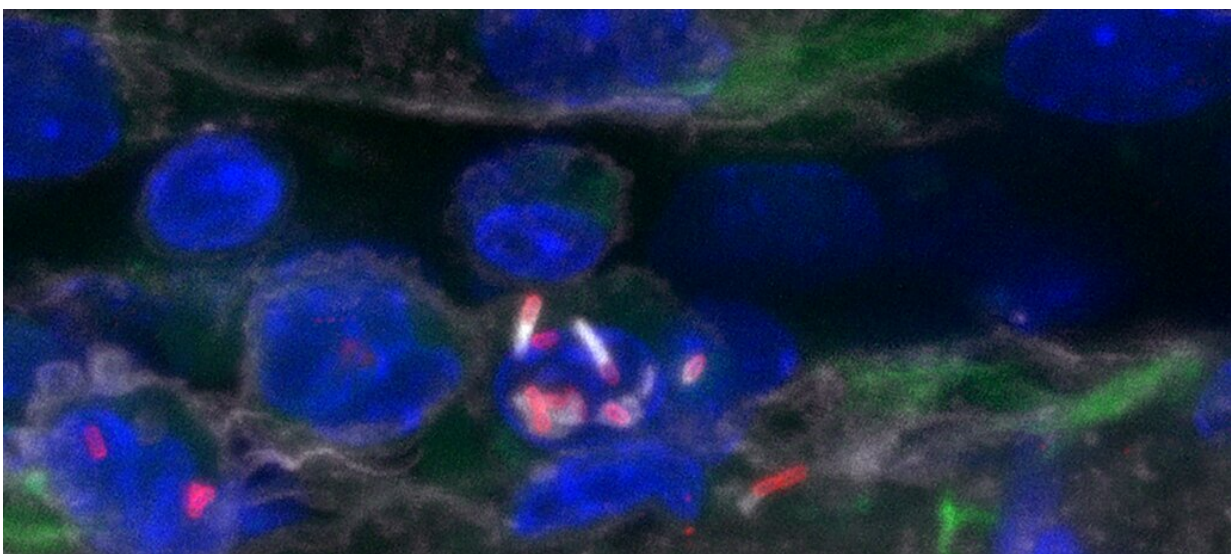


# Discovery of an immune escape mechanism promoting *Listeria* infection of the central nervous system

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Section of a cerebral vessel in an infected animal model containing infected monocytes adhering to endothelial cells. *Listeria* is marked in red, actin in white (including the actin tails propelling *Listeria*), nuclei in blue and macrophages in green. Credit: © Biology of Infection Unit - Institut Pasteur

Some hypervirulent strains of *Listeria monocytogenes* have a greater capacity to infect the central nervous system. Scientists from the Institut Pasteur, Université Paris Cité, Inserm and the Paris Public Hospital Network (AP-HP) have discovered a mechanism that enables cells

infected with *Listeria monocytogenes* to escape immune responses. This mechanism provides infected cells circulating in the blood with a higher probability of adhering to and infecting cells of cerebral vessels, thereby enabling bacteria to cross the blood-brain barrier and infect the brain. The study will be published in *Nature* on March 16, 2022.

The central nervous system is separated from the bloodstream by a physiological barrier known as the [blood-brain barrier](#), which is very tight. But some pathogens manage to cross it and are therefore able to infect the central nervous system, using mechanisms that are not yet well understood.

*Listeria monocytogenes* is the bacterium responsible for human listeriosis, a severe foodborne illness that can lead to a central nervous system infection known as neurolisteriosis. This central nervous system infection is particularly serious, proving fatal in 30% of cases.

Scientists from the Biology of Infection Unit at the Institut Pasteur (Université Paris Cité, Inserm) and the *Listeria* National Reference Center and WHO Collaborating Center led by Marc Lecuit (Université Paris Cité and Necker-Enfants Malades Hospital (AP-HP)) recently discovered the mechanism by which *Listeria monocytogenes* infects the [central nervous system](#). They developed a clinically relevant experimental model that reproduces the different stages of human listeriosis, [and involves virulent strains](#) of *Listeria* isolated from patients with neurolisteriosis.

The scientists first observed that inflammatory monocytes, a type of white blood cell, are infected by the bacteria. These infected monocytes circulate in the bloodstream and adhere to the cerebral vessels' cells, allowing *Listeria* to infect the brain tissue.

The research team then demonstrated that InIB, a *Listeria*

monocytogenes surface protein, enables the bacteria to evade the [immune system](#) and survive in the protective niche provided by the infected monocytes. The interaction between InIB and its cellular receptor c-Met blocks the [cell death](#) mediated by cytotoxic T lymphocytes, which specifically target Listeria-infected cells. InIB therefore enables infected cells to survive cytotoxic T lymphocytes.

This mechanism extends the [life span](#) of infected cells, raising the number of infected monocytes in the blood and facilitating bacterial spread to host tissues, including the brain. It also favors the persistence of Listeria in the gut tissue, its fecal excretion and transmission back to the environment.

"We discovered a specific, unexpected mechanism by which a pathogen increases the life span of the cells it infects by specifically blocking an immune system function that is crucial for controlling infection," explains Marc Lecuit (Université Paris Cité and Necker-Enfants Malades Hospital (AP-HP)), head of the Biology of Infection Unit at the Institut Pasteur (Université Paris Cité, Inserm).

It is possible that other intracellular pathogens such as *Toxoplasma gondii* and *Mycobacterium tuberculosis* use similar mechanisms to infect the brain. Identifying and understanding the immune escape mechanisms of infected cells could give rise to new therapeutic strategies to prevent infection and also pave the way for new immunosuppressive approaches for organ transplantation.

**More information:** Marc Lecuit, Bacterial inhibition of Fas-mediated killing promotes neuroinvasion and persistence, *Nature* (2022). [DOI: 10.1038/s41586-022-04505-7](https://doi.org/10.1038/s41586-022-04505-7).  
[www.nature.com/articles/s41586-022-04505-7](https://www.nature.com/articles/s41586-022-04505-7)

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