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# Do bacterial pathogens exploit exogenous siderophores to proliferate within host cells?

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## Résumé

Iron is an essential nutrient for bacterial growth but is tightly restricted in the host during infection by nutritional immunity and competition with the microbiota<sup>1,2</sup>. To overcome this limitation, many enteric pathogens rely on siderophores, small molecules that bind iron with high affinity. Pathogens can either produce their own siderophores or exploit those produced by other microorganisms present in their environment. Comparative genomic analyses performed in this work show that most antibiotic-resistant enteric pathogens encode multiple siderophore uptake systems, suggesting flexible iron acquisition strategies depending on environmental conditions. Consistently, we previously observed that under acidic conditions mimicking the intestinal environment, *Salmonella enterica* shifts iron acquisition toward the exploitation of exogenous siderophores, largely because endogenous siderophore production decreases<sup>3</sup>.

Despite the widespread ability of bacterial pathogens to utilize multiple siderophores, it remains unclear whether exogenous siderophore exploitation contributes to iron acquisition during intracellular infection. This project aims to determine if intracellular *Salmonella* can sense and exploit exogenous siderophores and whether this strategy supports bacterial proliferation within host cells. We further investigate how iron availability and iron acquisition strategies vary across distinct intracellular niches, including vacuolar and cytosolic environments, using infection models in epithelial cells and macrophages. Understanding how pathogens acquire iron across different infection environments is essential to better predict their behavior within the host and may help identify new therapeutic targets.

1. Murdoch, C.C., and Skaar, E.P. (2022). Nutritional immunity: the battle for nutrient metals at the host-pathogen interface. *Nat Rev Microbiol* 20, 657–670. <https://doi.org/10.1038/s41579-022-00745-6>.
2. Caballero-Flores, G., Pickard, J.M., and Núñez, G. (2023). Microbiota-mediated colonization resistance: mechanisms and regulation. *Nat Rev Microbiol* 21, 347–360. <https://doi.org/10.1038/s41579-022-00833-7>.
3. Ferry, M., Sharp, C., Schalk, I.J., and Cunrath, O. (2026). *Salmonella* relies on siderophore exploitation at low pH. *MicroLife* 7, uqaf041. <https://doi.org/10.1093/femsml/uqaf041>.

**Mots-Clés:** iron, nutritional immunity, enteric pathogens, siderophores, intracellular infection

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