Role of the chaperone HSP90 on siderophore biosynthesis in Pseudomonas aeruginosa

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Résumé

As iron is an essential nutrient for almost all living organisms and is poorly bioavailable, its acquisition is a highly regulated process. To harvest iron from the environment, bacteria produce iron-chelating proteins called siderophores. In *Pseudomonas aeruginosa*, the biosynthesis of its main siderophore, pyoverdine, involves four non-ribosomal peptide synthetases (NRPSs) named PvdD, PvdI, PvdJ and PvdL and other enzymes such as PvdA, PvdF, PvdH and form together a multi-enzymatic complex located into the cytoplasm and anchored to the membrane called siderosome (Schalk, 2025). The heat-shock protein 90 (HSP90) is a chaperone protein well studied in eucaryotes and linked to pathogenicity and virulence in some bacteria (Grudniak *et al.*, 2018). Preliminary data showed that some NRPS are client protein of the HSP90, suggesting its implication in the formation of the siderosome and thus in siderophore synthesis. To study this question, a mutant DHSP90 deleted from the gene encoding the chaperone protein was constructed and tested for PVD production, confirming the reduction of pyoverdine production in the absence of the chaperone. Supernatants were analyzed by MALDI-TOF and showed no difference in the pyoverdine structure produced by the wt and DHSP90 strains. To investigate how the absence of the chaperone impacts the localization of the NPRS and siderosome, cellular fractionation was carried out on *P. aeruginosa* DHSP90 tagged-NRPS. In parallel, we also conducted cell free protein synthesis of NRPS to determine *in vitro*, if the chaperone has an effect on the folding on one of the NRPS. This combination of *in vivo* and *in vitro* approaches will highlight the role of HSP90 on pyoverdine synthesis and *P. aerignosa* virulence.

Schalk, I. J. (2025). Bacterial siderophores: diversity, uptake pathways and applications. *Nature Reviews Microbiology*, *23*(1), 24-40.

Grudniak, A. M., Klecha, B., & Wolska, K. I. (2018). Effects of null mutation of the heat-shock gene htpG on the production of virulence factors by Pseudomonas aeruginosa. *Future microbiology*, *13*(1), 69-80.

Mots-Clés: Siderosome, HSP90, Pseudomonas aeruginosa, pyoverdine

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