Interaction of the Hfq protein with the bacterial membrane and functional consequences on RNA export

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THÈSE

Hfq is a pleiotropic bacterial regulator involved in several aspects of RNA metabolism. In particular, the protein regulates translation efficiency and RNA degradation in Gram-negative bacteria. It also facilitates the pairing of small regulatory non-coding RNAs (sRNAs) with their target messenger RNA (mRNA), usually via biding around the ribosome binding site (RBS) of the mRNA and/or the initiation codon. This enables a regulation at the post-transcriptional level, usually in a negative way. Post-transcriptional modulation of gene expression can thus affect the adaptation of bacteria to changing environments, which may be of paramount importance for the control of cell division, quorum sensing or the virulence of pathogenic species. Results obtained prior this thesis demonstrated that the C-terminal region of Hfq forms an amyloid-like structure that interacts with membranes. The immediate consequence of this interaction is membrane rupture, but the effect of the membrane on the amyloid structure was unknown.

This thesis work highlights the characterization of the mechanism of interaction with the bacterial membrane via various innovative biophysical techniques (such as Oriented Circular Dichroism or Polarized Fourier Transform Infrared Spectroscopy). With these different methods, it was possible to prove that the C-terminal part of the Hfq protein was inserted into the bacterial membrane at very precise locations, rich in cardiolipin. It is also proposed that Hfq can play an important role in cellular communication thanks to its presence in external membrane vesicles (OMVs), secreted into the extracellular milieu. The therapeutic aspect was also addressed in this thesis, with the identification of the role of Hfq in antibiotic resistance, but also the characterization of effective inhibitors targeting the amyloid structure.

Thanks to the various results contained in this work, this thesis opens the door to the study of new antibacterial approaches, aiming at destabilizing bacteria in their quest for antibiotic resistance.

Jury members:

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Vous êtes cordialement invités au pot qui suivra

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