Membrane barrier and drug translocation: Molecular approaches and imaging of antibiotic travel through bacterial envelope

Jean-Marie PAGES

[1] UMR-MD1, Aix-Marseille Université, IRBA, Marseille, France

Abstract

With the continuing emergence of bacterial multidrug resistance, a molecular dissection of the drug transport associated with cellular imaging analysis is needed to understand the Influx and Efflux and the activity of antimicrobial agents in bacterial cells. This is particularly acute for Gram-negative bacteria that have two membranes, outer and inner membranes, controlling the transport and the intracellular accumulation of antibiotics. The permeation process was followed within bacterial population and at a single bacteria level to investigate the antibiotic concentration/location in multi-drug resistant isolates. Antibacterial activities were determined on same bacterial strains in order to correlate the intracellular accumulation of antibiotic to the bacterial susceptibility.

With this original methodology that combines UV fluorescence microscopy, mass spectrometry, clinically used antibiotics or original molecules, clinical isolates and derivative strains, in the absence or in the presence of chemosensitizers, the accumulation of antibiotics can be studied in bacteria. The respective involvement of influx and efflux in the internal concentration of various molecules and in the bacterial susceptibility can be determined and compared in various strains. Two concepts are emerging describing the "structure-intracellular concentration activity relationship" that addresses the drug structure and the "resident time concentration close to target" that depends on bacterial membrane permeability.

This methodology combination opens a new field of research in the molecular understanding of membrane-associated mechanisms of resistance and in the rational approach of antibacterial chemotherapy

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