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Membrane protein platforms for metal efflux in some bacteria

Tuberculosis is caused by the bacterium Mycobacterium tuberculosis (Mtb). Upon infection, the pathogen is phagocyted by macrophages, the sentinel cells of the immune system. In the macrophage, Mtb accumulates in the phagosomes where it must adapt to cope with toxic concentrations of metals such as zinc. In that context, metal poisoning can be seen as a host defence mechanism to regulate/eliminate the pathogen.
In 2011, the team led by Olivier Neyrolles at the Institut de Pharmacologie et de Biologie Structurale (Toulouse) demonstrated that the survival of Mtb in phagosomes required a membrane transporter belonging to the P-ATPase family. This transporter called CtpC would export the zinc in excess from Mtb cytoplasm (1)

In the present study (2), we demonstrate that CtpC is not functional in mycobacterial membranes if PacL1 (P-ATPase-associated chaperone-Like protein 1), a small membrane protein of previously unknown function is absent. PacL1 colocalizes with CtpC at microdomains in the bacterial membrane and has a zinc binding motif at its C-terminus. Without PacL1, CtpC is no longer localized at the membrane and M. tuberculosis becomes highly sensitive to zinc. In this study, we identified two other P1B-ATPases/PacL pairs in M. tuberculosis involved in metal transport: CtpG/PacL2 and CtpV/PacL3. In addition, other P-ATPases/PacL pairs are also found in different types of bacteria.

This work suggests that metal resistance in some bacteria may use membrane platforms combining P-ATPases and small PacL-type chaperones, a new concept in the metallobiology of prokaryotes.

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Session

Host-pathogen interactions

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