Mycobacterial lipoproteins – synthesis, structure and their role in virulence

Peter Sander, Andreas Tschumi, Petra Selchow, Peter Keller, Silke Polsfuss, Juliane Brülle, Tobias Rosenberger, Agnese Petrera, Beat Amstutz, Thomas Grau

Institute of Medical Microbiology, University of Zurich, Zurich, Switzerland

Lipoproteins are ubiquitously present in bacteria and attached to the cell surface by a lipid anchor. They build a heterogeneous class of proteins involved in a variety of functions including cell wall synthesis, nutrient uptake, drug resistance and virulence. Lipoproteins mature by post-translational modifications through the consecutive activity of two (Gram-positive bacteria) or three enzymes (Gram-negative bacteria), phosphatidylglycerol:pre-prolipoprotein diacylglycerol transferase (Lgt), prolipoprotein signal peptidase (LspA) and eventually phospholipid:apolipoprotein *N*-acyltransferase (Lnt) (1).
The genome of *Mycobacterium tuberculosis* encodes approximately 100 lipoproteins. The majority of these do not yet have an annotated function. A *M. tuberculosis* mutant deficient in lipoprotein modification (*ΔlspA*) is highly attenuated in animal models of tuberculosis: the mutant barely replicates in lungs of infected mice and does not spread to secondary organs. Thus, lipoprotein synthesis is an important virulence factor of tuberculosis (2, 3). Using *Mycobacterium smegmatis* as a model we now characterized the lipid structure of the *M. tuberculosis* lipoprotein LppX at the molecular level. Mycobacterial lipoproteins are modified with *Mycobacterium* specific fatty acids. Moreover, although belonging to the group of Gram-positive bacteria mycobacterial lipoproteins are *N*-acylated by an enzyme homologous to *Escherichia coli N*-acyltransferase (Lnt) (4).

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