Comprehensive proteome analysis of Mycobacterium ulcerans and quantitative comparison of mycolactone biosynthesis

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Résumé en anglais	Mycobacterium ulcerans is the causative agent of Buruli ulcer, a rapidly emerging human disease in which mycolactone, a cytotoxic and immunosuppressive macrocyclic polyketide, is responsible for massive skin destruction. The genome sequencing of M. ulcerans has recently been accomplished (http://genolist.pasteur.fr/BuruList/ [12]) enabling the first proteome study of this important human pathogen. Here, we present a comprehensive proteome analysis of different subcellular fractions and culture supernatant of in vitro grown M. ulcerans. By a combination of gel-based and gel-free techniques for protein and peptide separation with subsequent analysis by MS, we identified 1074 different proteins, corresponding to 25% of the protein-coding DNA sequence. Interestingly, new information was obtained about central metabolism and lipid biosynthesis, and as many as 192 conserved hypothetical proteins were found. Comparative analysis of the wild-type strain and an isogenic mycolactone-deficient mutant, by 2-DE and iTRAQ labeling of the cytoplasmic fraction, revealed differences in the expression profiles of proteins involved in lipid metabolism and information pathways, as well as stress responses.
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