



Genomics of glycopeptidolipid biosynthesis in *Mycobacterium abscessus* and *M. chelonae*

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BACKGROUND: The outermost layer of the bacterial surface is of crucial importance because it is in constant interaction with the host. Glycopeptidolipids (GPLs) are major surface glycolipids present on various mycobacterial species. In the fast-grower model organism *Mycobacterium smegmatis*, GPL biosynthesis involves approximately 30 genes all mapping to a single region of 65 kb.

RESULTS: We have recently sequenced the complete genomes of two fast-growers causing human infections, *Mycobacterium abscessus* (CIP 104536T) and *M. chelonae* (CIP 104535T). We show here that these two species contain genes corresponding to all those of the *M. smegmatis* "GPL locus", with extensive conservation of the predicted protein sequences consistent with the production of GPL molecules indistinguishable by biochemical analysis. However, the GPL locus appears to be split into several parts in *M. chelonae* and *M. abscessus*. One large cluster (19 genes) comprises all genes involved in the synthesis of the tripeptide-aminoalcohol moiety, the glycosylation of the lipopeptide and methylation/acetylation modifications. We provide evidence that a duplicated acetyltransferase (*atf1* and *atf2*) in *M. abscessus* and *M. chelonae* has evolved through specialization, being able to transfer one acetyl at once in a sequential manner. There is a second smaller and distant (*M. chelonae*, 900 kb; *M. abscessus*, 3 Mb) cluster of six genes involved in the synthesis of the fatty acyl moiety and its attachment to the tripeptide-aminoalcohol moiety. The other genes are scattered throughout the genome, including two genes encoding putative regulatory proteins.

CONCLUSION: Although these three species produce identical GPL molecules, the organization of GPL genes differ between them, thus constituting species-specific signatures. An hypothesis is that the compact organization of the GPL locus in *M. smegmatis* represents the ancestral form and that evolution has scattered various pieces throughout the genome in *M. abscessus* and *M. chelonae*.

Résumé en anglais

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