The mycobacterial glucosylglycerate hydrolase is restricted to rapidly growing species

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The majority of the 156 known species of Mycobacterium was isolated from the environment and designated nontuberculous mycobacteria (NTM). They are ubiquitous inhabitants of soils and waters but frequently established in man-made water distribution systems and hospitals (1). The rising numbers of atypical infections by opportunistic NTM and drug/disinfectant-resistant strains of rapidly growing species (RGM) like M. abscessus claim for urgent measures to fight these pathogens (2).

The adaptive success of Mycobacterium spp. is intimately associated to a unique lipid-rich cell wall. They also synthesize a specialized class of methylated polysaccharides that serve as lipid carriers: the methylglucose lipopolysaccharides (MGLPs) and methylmannose polysaccharides (MMPs), which accommodate fatty acids and regulate their synthesis (3). MGLPs synthesis has glucosylglycerate (GG) as primer and, in most organisms using it for osmoadaptation GG is synthesized via a phosphorylated intermediate through the consecutive action of a specific glucosyl-3-phosphoglycerate synthase (GpgS) and a glucosyl-3-phosphoglycerate phosphatase (GpgP) (4). In mycobacteria, these reactions are catalyzed by non-homologous isofunctional versions of GpgS and GpgP (5, 6).

We have now identified a mycobacterial enzyme that specifically hydrolyses GG to glucose and glycerate (GG hydrolase, GgH). The recombinant GgH from M. hassiacum was stable and optimally active at 42ºC and pH 5.5 with Mg2+ and KCl significantly enhancing activity and stability. The corresponding ggH gene was almost exclusively found in genomes of RGM. Since GG was shown to accumulate in nitrogen-starved M. smegmatis (7), we propose that GgH is involved in the recycling of GG accumulated during N-starvation.

Genetic and biochemical dissection of a novel mycobacterial pathway will contribute to a deeper understanding of these organisms’ physiology and lifestyle and reveal new strategies to fight infections caused by these ubiquitous and resilient pathogens.

Keywords: Mycobacterium, methylglucose lipopolysaccharides, glucosylglycerate, hydrolase.

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