Poster Presentation

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Molecular details of sugar biosynthesis in mycobacteria

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Despite the research efforts of decades, Mycobacterium tuberculosis is still in the origin of 1.3 million deaths annually (WHO, Tuberculosis, 2013) and is estimated to infect 2 billion people worldwide. The currently available antimicrobial therapies are aimed at only a few molecular targets and the growing number of strains resistant to multiple drugs drives an urgent need for the identification of novel pathways and new points for therapeutic intervention. Although the sequence of the M. tuberculosis genome has been known for more than a decade, there is still no function assigned to many of its genes. Among M. tuberculosis ORFs with known function, more than 1% encode enzymes involved in glycosidic bond synthesis. Since the increased resilience of M. tuberculosis is, to a great extent, due to its complex, polysaccharide/lipid-rich and thus unusually impermeable cell wall, we became interested on the functional and structural characterization of mycobacterial enzymes involved in biosynthetic pathways for cell wall components. Over the last few years, we have carried out the functional and structural characterization of novel enzymes in the sugar biosynthesis metabolic routes from thermostable and mesostable mycobacteria [1-3]. Recently, we characterized functionally two enzymes from M. vanbalenii and M. hassiacum whose orthologs in M. tuberculosis are essential for growth, and determined their three-dimensional structures to high resolution (1.2-1.5 Å), allowing the thorough elucidation of their intricate nucleotide and sugar specificities. These experimental molecular models will be presented as examples of frameworks for the rational design of novel anti-mycobacterial drug leads. (Funded by national funds through FCT and by EU-FEDER funding through COMPETE (grants FCOMP-01-0124-FEDER-014321, FCOMP-01-0124-FEDER-014187, FCOMP-01-0124-FEDER-028359) and through ON.2-O Novo Norte, under QREN (grant NORTE-07-0124-000002 - Host-Pathogen Interactions).

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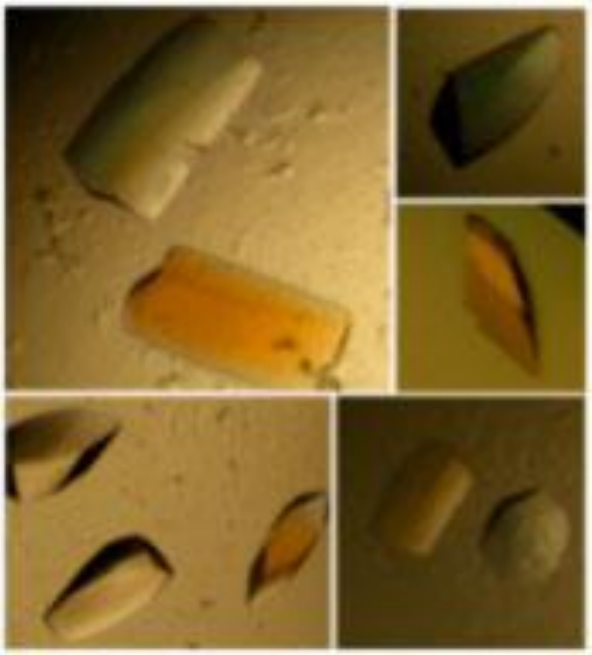

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