Project 1

Title: The pneumococcal metabolome in response to different host sugars

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Host laboratory: Lactic Acid Bacteria & in vivo NMR

Short description:

Streptococcus pneumoniae is a major human pathogen that causes serious diseases, such as pneumoniae, bacteraemia, and meningitis. The knowledge of *in vivo* physiology and metabolism of *S. pneumoniae* is limited, even though to a large extent the pneumococcal pathogenesis relies on efficient acquisition and metabolism of the nutrients required for growth and survival. Being a strictly fermentative organism, the ability to take up and metabolize sugars is of chief importance. The preferred sugar source of *S. pneumoniae* is scarce in its most common habitat, the human nasopharynx. In this environmental niche, mucus host glycoproteins (mucins) are most likely the major source of sugars for growth. S. pneumoniae is equipped with exoglycosidases capable of degrading mucins to free mono and disaccharides, and we have established growth profiles in different mucin-derived sugars as well as sugar mixtures.

In this work, we aim at determining the pneumococcal metabolome in the presence of different sugars and or sugar/mixtures. We will employ optimized quench and extraction methods to prepare metabolite samples. We will use standard 1D- (1H, 13C and 31P) and 2D-NMR (1H/13C-COSY, 1H/31P-COSY, HSQC, etc.) techniques for metabolite profiling and identification. Additionally, analysis of cell extracts will be performed in an LC-MS/MS platform that allows quantifying absolute concentrations for 50-80 central metabolic intermediates (EHT Zurich). The data obtained will be used as input to develop a mathematical model of mucin-derived sugars metabolism. We expect that this model will provide insight into which factors in sugar assimilation essential to thrive in the different host niches. Ultimately, this information can assist in discovering potential discovering potential drug targets in *S. pneumoniae*. This work is in line with that of an FCT funded project PTDC/SAU-MII/100964/2008.

Duration: 1 year.