BIOTRANS
LA ROCHELLE 2023

N°393 / OC / PC
TOPIC(s) : Enzyme discovery and engineering / Synthetic biology, metabolic engineering

Glycoside-phosphorylases: in vitro and in cellulo implementation for the production of valuable glycosides

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PURPOSE OF THE ABSTRACT

Glycoside Phosphorylases (GPs) are reversible Carbohydrate Active Enzymes enzymes able to degrade glycosides thanks to inorganic phosphate (phosphorolysis) or to synthesize glycosides thanks to sugar-phosphates and adequate acceptors (reverse phosphorolysis) [1]. Without the need of costly activated-sugars, they can be used to produce valuable glycosides. Such biocatalysts represent a solid alternative to natural extraction and chemical synthesis, which suffer from low yield, lack of structural purity, high energy-use and sustainability issues [2]. However, the reverse phosphorolysis reaction is difficult to exploit at industrial scale because of the high cost and limited commercial availability of sugar-phosphates, as well as unfavourable reaction equilibria. Those limitations can be overcome by implementing GPs in engineered microbial cells. The cells can provide substrates for reverse phosphorolysis, and promote GP synthesis by displacing the reaction equilibrium with secretion of the products of interest. For that, the microbial chassis must be able to accumulate cytoplasmic sugar-phosphates, which can be achieved by metabolic engineering. The proof of concept of this technology was made in an engineered Escherichia coli K12 strain [3] that ultimately was able to synthesize β-mannosides (β-MOS) of pharmaceutical interest once transformed with mannoside phosphorylases from the GH130 family. Notably, mannosides linked with β-1,2 linkages (β-1,2-MOS) are antigenic patterns of the pathogenic yeast Candida [4]. They can be used to prevent and cure candidiasis, an infectious disease affecting more than 300 million patients per year, and possibly lethal in its most serious form [5]. Implemented in engineered microbial cells or used in vitro, GPs are powerful tools to access a wide range of glycosides previously unreachable, and will undoubtedly be significant players in the coming years.

FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

Glycoside Phosphorylases | Mannosides | Metabolic engineering

BIBLIOGRAPHY