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Enhancing the production of mannosylglycerate in *S. cerevisiae* through *in silico* driven metabolic engineering

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Mannosylglycerate (MG) is a compatible solute with major potential applications in the cosmetic industry, as moisturizer and skin protector against UV damage, storage of vaccines and other biomaterials, or protein stabilizer in analytical and clinical kits. Since the production of MG is expensive the development of efficient production systems is mandatory to fully exploit the potential of this solute. *Saccharomyces cerevisiae* was selected to produce MG, which is synthesized by the condensation of GDP-mannose and 3-phosphoglycerate. To better understand the impact of this pathway in yeast metabolism, the two enzymatic reactions were accommodated and evaluated *in silico* using the yeast genome scale metabolic model *i*MM904. Several optimization algorithms were ran to find the sets of genetic modification that lead to maximization of MG production. Results show that the production can be optimized by increasing the flow towards GDP-mannose formation and by introducing a bottleneck in the synthesis of pyruvate. This metabolic engineering strategy that targets the increased supply of biosynthetic precursors was implemented *in vivo*. Results show that MG accumulation increases 1.5-fold by overexpressing the genes involved in formation of GDP-mannose. However, no effect in the production of MG was observed when 3-phosphoglycerate was overproduced. Moreover, higher yields of MG were obtained when the mutants were cultivated in chemostast in comparison with batch mode.