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Engineering carbon-conserving synthetic pathways for assimilation and conversion of C5/C6 carbon sources into added value chemicals

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The development of carbon efficient pathways for added value (bio)chemicals production is the essence of White Biotechnology. The limit of carbon conservation in all (bio)chemical syntheses is determined by the electron balance in substrate(s) and product(s). Frequently, natural metabolic networks do not have the stoichiometric capacity to produce a value-added compound at yields that correspond to the thermodynamic maximum. A good example of natural metabolic networks lacking stoichiometric efficiency is the bioproduction of glycolic acid (GA), a two carbon compound of considerable industrial interest notably in cosmetics and biodegradable polymers. We addressed this objective to approach this maximal conversion yield by employing the following strategies. Firstly, we reconsider a completely different route of C5 assimilation that by-passes the decarboxylation reaction in the pentose phosphate pathway and that rely on the carbon-conserving aldolytic cleavage of X1P or R1P to yield the C2 compound glycolaldehyde and the C3 DHAP compound. This metabolic scheme required the expression of human hexo(fructo)kinase(Khk-C) and human aldolase (Aldo-B). Then glycoaldehyde can be either reduced by endogenous aldehyde reductase to produce ethylene (EG) glycol or oxidized into glycolic acid. With this approach, we obtained yield of EG and GA close to maximal theoretical yield of 1 mol/ mol sugar. Interestingly, we found that the engineered strain expressing this synthetic pathway exhibited a remarkable rewiring of the metabolic networks that culminate with a dramatic reduced metabolites and metabolic energy levels. We then combined this synthetic pathway with the natural glyoxylate shunt that can be engineered to produce GA from DHAP. This combination led to an optimized production strain that produced ~30 % more GA from a xylose/glucose mixture (66%/33%) than when the natural pathway is working alone.

Biography

Jean M François got his PhD in Biological Science and Agronomy from the University of Louvain (Belgium) in 1988. He is Professor of Industrial Microbiology and BioNanotechnology at the Federal University of Toulouse, School of Engineer. His research activity concerns integrated physiology and functional genomics in microbial systems, with a specific focus on carbon and energy metabolism in yeast and filamentous fungi . He is author of more than 180 papers and 15 patents and Editor in Chief of BMC Biotechnology for Biofuels.

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