

SYSTEMS METABOLIC ENGINEERING OF CORYNEBACTERIUM GLUTAMICUM AND BACILLUS METHANOLICUS FOR PRODUCTION OF NEW PRODUCTS FROM ALTERNATIVE CARBON SOURCES

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Amino acid production amounts to about 2 million tons of L-lysine and 3 million tons of L-glutamate per year [1]. *Corynebacterium glutamicum* is widely used in industry for amino acid production from sugars, while the methylotrophic *Bacillus methanolicus* produces L-lysine and L-glutamate from methanol with titers of about 50 g/L [2]. Both microbial hosts have been developed for production of specialty amino acids and amines. Specifically, I will present new tools for metabolic engineering of *B. methanolicus* and *C. glutamicum* including CRISPRi/dCas9, sigma factor engineering, genome reduction, induction with photocaged IPTG, theta-type replicating vectors and biosensors [3-10]. On the other hand, I will describe examples of metabolic engineering of these hosts for the production of specialty amino acids and diamines. *C. glutamicum* strains for the production of L-pipecolic acid have been constructed [11] and these were improved a titer of 14.4 g L⁻¹, a volumetric productivity of 0.21 g L⁻¹ h⁻¹ and an overall yield of 0.20 g g⁻¹ [12]. Moreover, access to production of L-pipecolic acid from glucose, glycerol, xylose, glucosamine, and starch has been enabled. Methanol-based production of the non-proteinogenic amino acid γ -amino butyric acid (GABA), that finds application also as precursor for bioplastics, has been achieved with *B. methanolicus* [13]. Efficient production of GABA from hexose and pentose sugars has been realized and optimized in recombinant *C. glutamicum* strains as well [14,15]. Both for *C. glutamicum* and *B. methanolicus* characterization and engineering of product export have been instrumental [16,17].

In conclusion, the microbial cell factories *B. methanolicus* and *C. glutamicum* have been programmed for efficient and sustainable production of specialty amino acids and amines from diverse carbon feedstocks to foster their biotechnological applications.

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