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Klebsiella pneumoniae as cell factory for chemicals production

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Klebsiella pneumoniae is an important industrial microorganism and can utilize a wide range of different carbon sources including glucose, xylose, and glycerol for production of many chemicals. In addition, various molecular biological tools are available for metabolic pathway engineering. This makes *K. pneumonia* an excellent candidate as cell factory for production of chemicals with industrial applications such as 1,3-propanediol, 2,3-butanediol, acetoin, isobutanol and 2,3-dihydroxyisovalerate. It has been shown that *K. pneumoniae* is an efficient 1,3-propanediol producer and the technology using glycerol as a feedstock has been industrialized in China. More recently a *K. pneumoniae* Δ*tpiA* knock-out strain was constructed that lost the activity of triosephosphate isomerase and prevented glycerol catabolism. However, this strain still utilized glycerol, and 1,2-propanediol became the main catabolite [1]. Using glucose or other sugars as carbon sources, 2,3-butanediol is the main product of this bacterium. 2,3-butanediol has three stereoisomers, and all isomers can be synthesized by *K. pneumoniae* [2]. By disruption of butanediol dehydrogenase and culturing the engineered strain with glucose as the carbon source R-acetoin was produced in high titers [3]. The 2,3-butanediol synthesis pathway and branched-chain amino acid synthesis pathway share the same step of α-acetolactate synthesis from pyruvate. Blocking the 2,3-butanediol synthesis pathway by knocking out *budA* resulted in higher α-acetolactate flow into the branched-chain amino acid synthesis pathway, and 2-ketoisovalerate was produced by this engineered strain. 2-ketoisovalerate is converted to isobutyraldehyde with the catalysis of an indole-3-pyruvate decarboxylase (*ipdC*), and isobutyraldehyde is further converted to isobutanol (Fig. 1). This is the first endogenous isobutanol synthesis pathway identified in bacteria [4]. In the branched-chain amino acid synthesis pathway, 2-ketoisovalerate is synthesized from 2,3-dihydroxyisovalerate with the catalysis of dihydroxy acid dehydratase (*ilvD*). The *ilvD* knock out strain produced a high level of 2,3-dihydroxyisovalerate, providing the first biological production route [5]. Our work demonstrates that *K. pneumonia* has great potential as cell factory for chemicals production and industrially relevant titres and yields can be obtained by metabolic pathway engineering and optimization of fermentation conditions.

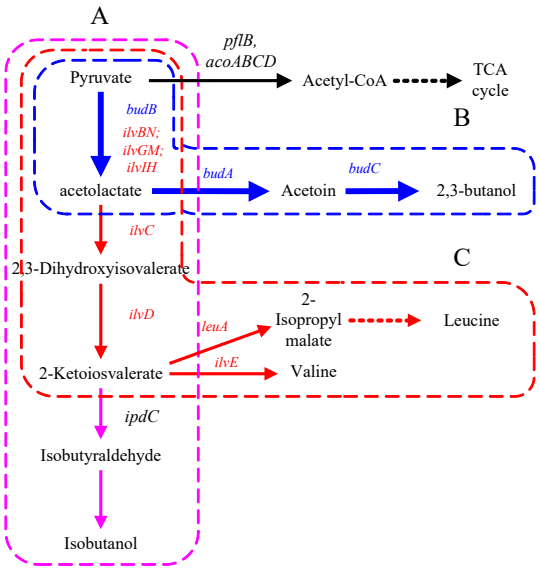

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Figure 1: A) Native isobutanol synthesis pathway in K. pneumoniae. B) 2,3-butanediol synthesis pathway. C) Branch amino acid synthesis pathways.