Systems strategies for developing industrial microbial strains.

Industrial strain development requires system-wide engineering and optimization of cellular metabolism while considering industrially relevant fermentation and recovery processes. It can be conceptualized as several strategies, which may be implemented in an iterative fashion and in different orders. The key challenges have been the time-, cost- and labor-intensive processes of strain development owing to the difficulties in understanding complex interactions among the metabolic, gene regulatory and signaling networks at the cell level, which are collectively represented as overall system performance under industrial fermentation conditions. These challenges can be overcome by taking systems approaches through the use of state-of-the-art tools of systems biology, synthetic biology and evolutionary engineering in the context of industrial bioprocess. Major systems metabolic engineering achievements in recent years include microbial production of amino acids (L-valine, L-threonine, L-lysine and L-arginine), bulk chemicals (1,4-butanediol, 1,4-diaminobutane, 1,5-diaminopentane, 1,3-propanediol, butanol, isobutanol and succinic acid) and drugs (artemisinin).