### SYSTEMS BIOTECHNOLOGY

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Systems biology has been changing the way biological and biotechnological research is performed. Now, systems biological approaches can be taken to develop bioprocesses for the production of valuable drugs, commodity and fine chemicals, fuels, and polymers and other materials; this is termed systems biotechnology. Here I present the general strategies for systems biotechnology and several examples of applying systems biotechnological strategies for the development of bioprocesses for the efficient production of chemicals and materials. This also includes a strategy of systems metabolic engineering for the development of microbial strains. It is expected that systems biotechnology will be at the heart of successful industrial biotechnology towards low carbon green growth of the world

Keywords: systems biology; systems biotechnology; metabolic engineering; industrial biotechnology

#### 1. Strategy of Systems Biotechnology

Systems biotechnology [1] can be defined, following the OECD definition of biotechnology, as the application of science and technology at systems level to living organisms as well as parts, products and models thereof, for the production of knowledge, goods and services. As we become equipped with many experimental and computational tools and methods, we can better understand the cell as a whole. A typical bioprocess for the production of a desired product will rely on the choice of a main substrate (e.g., carbon source), development of superior microorganism through metabolic engineering, fermentation, and downstream processing for product recovery [2]. These unit processes need to be optimized in an integrated manner to achieve the best performing process [3]. Systems biology contributes significantly to the strain development through metabolic engineering; thus it is called systems metabolic engineering [3-5]. Of course, midstream (fermentation) and downstream processes need to be carefully examined so that strains can be further engineered for the best overall performance. This means that some of the problems encountered during the mid- to down-stream processes can be tackled by further metabolic engineering based on systems-level analysis [3,6].

### 2. Systems Metabolic Engineering

Systems metabolic engineering [3-6] allows purposeful modification of metabolic, gene regulatory, and signaling networks based on systems-level analysis. One can set the objective as enhanced production of a desired product, production of novel product, or

utilization of inexpensive carbon source, or all of these. In addition to all the tools and methods of metabolic engineering available, omics and computational methods [7,8] can be applied to the development of superior strains. Here I will give examples on the development of amino acid producers [4,6,9,10], diamine producer [11], succinic acid producer [12], and polymer producer [13,14] by systems metabolic engineering. If time permits, the strategies for drug target discovery by systems approach [15-17] will also be described.

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