Metabolite Valves for the Inducible, Dynamic Control of Glucose Metabolism in E. coli
Technology #12369

Applications

Metabolite valves are dynamic control systems that redirect metabolic flux in order to overproduce compounds of commercial value (e.g., industrial fuels, chemicals, pharmaceutical products) in a microbial system. By redirecting metabolic pathway activity—or “flux”—from endogenous to heterologous pathways, metabolite valves can switch between “growth mode” and “production mode,” respectively, thus enhancing yield and productivity without compromising host survival. Glucose valves, for example, act by redirecting glycolytic flux away from cell growth and into heterologous pathways in which glucose is used as the substrate for production (e.g., gluconic acid synthesis).

Problem Addressed

The engineered production of metabolic pathway components in microbial hosts is generally low-yield, in part due to competition with endogenous pathways. Strategies that involve the static knockdown of native genes often result in detrimental effects to host cells, including reduced growth and poor expression of recombinant proteins. Inducible promoter systems (i.e., metabolite valves) offer tunable control over metabolic flux, allowing for a “growth mode” and a “production mode,” thus balancing host health and heterologous pathway productivity.

Technology

This technology describes a strain of E. coli that has been engineered to redirect glucose metabolism for the purpose of overexpressing industrially relevant compounds. Glycolytic flux is endogenously determined and tightly regulated, thus limiting production in heterologous pathways. Metabolite valves inducibly redirect glucose away from glycolysis and into alternate pathways that use glucose as the substrate (e.g., glucaric acid production). The system utilizes an engineered E. coli strain in which glucose transport and phosphorylation are uncoupled. Redirection of glucose flux is determined based on expression levels of Glucokinase (Glk), which acts as the control hub. Downregulation of Glk via either antisense RNA or an inducible repressor opens the “valve,” thus shunting free glucose toward glucaric acid synthesis. In the “closed” state, glycolysis proceeds without interference and biomass production is prioritized.

Advantages

- Increased pathway yield of gluconic acid
- Reduced carbon waste
- Inducible, temporal regulation of metabolic flux
- Transcription-based regulation yields tight control over gene expression
- Utilizes glucose as an inexpensive carbon source
Related Technology

Dynamic Knockdown of E. Coli Central Metabolism for Redirecting Glucose-6-Phosphate Fluxes. Metabolite Valves for the Inducible, Dynamic Control of Glucose Metabolism in E. coli is related to Inducible, Dynamic Control System to Redirect Metabolic Flux in E. coli, Case number 17132.

Categories For This Invention:

Life Sciences
Biotechnology
Industrial/Energy
Chemicals
Biochemicals
Synthetic Biology
Bacterial

Intellectual Property:

Glucose valve and other metabolite valves
Issued US Patent
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Publications:

A Dynamic Metabolite Valve for the Control of Central Carbon Metabolism
Metabolic Engineering
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External Links:

Prather Research Group
http://web.mit.edu/prathergroup/

Image Gallery:
Figure 3: Design and implementation of the Glucose valve: TmP-P and PDPT downregulation. GluP-P

- TmP-P: downregulation of glucose phosphotransferase pathway
- PDPT downregulation of glucose phosphotransferase pathway

- GluP-P: downregulation of glucose phosphotransferase pathway

- TmP-P: downregulation of glucose phosphotransferase pathway

- PDPT downregulation of glucose phosphotransferase pathway

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