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Commentary

An Overview on Metabolite Secretion in Microorganisms

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DESCRIPTION

Microorganisms have been used for the production of industrially relevant compounds for many years. *Corynebacterium glutamicum* and its mutants have been employed for the large-scale industrial production of glutamate, lysine and other flavor active amino acids. Aspergillus niger is utilized for the fermentative production of citric acid, accounting for more than 90% of total citrate production worldwide. Another industrially significant metabolite, succinic acid, has been produced in large quantities by microorganisms including *Actinobacillus succinogenes, Corynebacterium glutamicum, Escherichia coli* and some genetically modified yeasts. Consequently, numerous studies have focused on the characterization of metabolic pathways and the development of tools to manipulate these pathways in order to increase product yield. Metabolite secretion is beneficial for industrial production as it simplifies the downstream extraction and purification of metabolites of interest.

The transport of substrates into the cell has been the subject of many researchs. Comparatively, very little is known about the mechanisms of secretion of intracellular metabolites, mainly primary metabolites. The secretion of metabolites is an essential biochemical function and reflects the inner metabolic state of the cell in response to environmental conditions. This process permits the removal of cell metabolic by-products from the intracellular medium in order to maintain homeostasis. Most metabolite secretions are believed to result from imbalanced intracellular metabolic pathways inflicting an overflow of pathway intermediates and secretion of these metabolites due to intracellular accumulation. Metabolic overflow is a phenomenon commonly observed in many microorganisms, commonly when the rate of glycolysis exceeds a critical value. Under fully aerobic and substrate-rich conditions, maximum microbial cells use inefficient metabolic routes and convert a considerable quantity of accessible carbon to incompletely oxidized end products together with ethanol, acetate and lactate. However, the concept of metabolic overflow cannot explain the secretion of many metabolites determined in time-series studies with parallel measurement of intracellular and extracellular metabolites.

We regularly observe some metabolites being directly excreted to the extracellular medium without intracellular accumulation in reaction to environmental cues. This scenario is most obvious when toxic metabolites are actively secreted by the cell using different efflux pumps. However, other metabolites can be secreted following intracellular metabolic overflow under one environmental condition while they are exported without intracellular accumulation under another. Both metabolic overflow and active efflux (secretion without an intracellular accumulation) processes are behind of metabolite secretion however, their mechanisms of regulation, especially when not following metabolic overflow, are still unclear. The study of microbial transport mechanisms has primarily focused on uptake systems.

CONCLUSION

Efflux transport has received much less attention despite its immense relevance to industrial processes. The exceptions are the study of multidrug efflux pumps in bacteria and fungi due to their role in drug-acquired resistance. The study of primary metabolite secretion mechanisms in microorganisms has been limited mostly to a handful of amino and non-amino organic acids of industrial interest. Efflux transport mechanisms are similar to those involved in metabolite uptake. The secretion or efflux of intracellular metabolites to outside the cell occurs through active or passive mechanisms. Passive transport is not concentrative in nature and it is rather equilibrative of transmembrane thermodynamic activities. Passive secretion is carried out either through the cell membrane (lipoidal diffusion) or with the help of transporters (facilitated diffusion). It occurs for most non-charged molecules and depends on the hydrophobicity of the solute and the properties of the membrane.

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