Regulation of glucose transport by the phosphotransferase system (PTS) in *E.coli*

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Five transporters belonging either to the PTS or non-PTS class can transport glucose in *E.coli* but the regulation of glucose transport remains unclear. To get insights into the possible regulatory mechanisms, we performed a FRET screen of interactions among cytoplasmic proteins and transporters involved in glucose transport. This screen revealed a network of interactions, with $EIIA^{glc}$ and $EIIBC^{glc}$ components of the glucose PTS interacting with non-PTS glucose/galactose transporters GalP and MglBAC. These interactions apparently depend on the phosphorylation state of the PTS components, indicating possible cross-regulation of different transport systems. Using galactose transport assays, we confirmed that the glucose PTS inhibits the uptake of galactose or glucose through galactose transporters. We believe that the function of such regulation might be to reduce the cost of glucose transport by the less energy-efficient systems.

Keywords – Phosphotransferase system, Glucose transport, $EIIA^{glc}$, MglA, $EIIBC^{glc}$.

I. Introduction

In changing environments selection of carbon source is extremely important for survival and growth. Catabolite repression and inducer exclusion are two known mechanisms that allow uptake of preferred sugars over the less preferred ones (1).

Repression of catabolic genes for a less preferred carbon source by a more preferred one is called catabolite repression. Inhibition of the uptake of less preferred carbon source by a more preferred one is called inducer exclusion (1). The phosphotransferase system (PTS) is central to both mechanisms (1,2). Inducer exclusion and catabolite repression effects of glucose on the non-PTS sugars are well studied, but less in known about regulation of glucose transport itself.

Glucose, mannose and maltose PTS transporters along with galactose non-PTS transporters, GalP and MglBAC, are known to transport glucose (2).

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We were interested in understanding whether and how the activities of these transporters might be regulated to ensure optimality of glucose uptake. In order to understand the possible regulatory mechanisms, we performed a FRET screen of interactions between the cytoplasmic proteins and transporters involved in glucose transport. We have further characterized these interactions and investigating their role in glucose transport.

II. Results

We observed a dense network of interactions between cytoplasmic proteins and transporters involved in glucose transport. Interactions between some of these proteins depend on their phosphorylation status. Components of the glucose PTS, $EIIA^{Glc}$ and $EIIBC^{Glc}$, interact with galactose transporters, GalP and MglBAC, and this interaction is apparently enhanced by dephosphorylation of PTS components. Furthermore, in case of GalP the interaction requires binding of its ligand galactose.

Interestingly, interaction of glucose PTS components ($EIIA^{glc}$ and $EIIBC^{glc}$) with galactose ABC transporter MglBAC occurs at lower glucose concentration than their interaction with galactose symporter GalP. We believe that the EC50 values of these interactions reflect the range in which glucose transport systems operate or cross regulate each other.

The role of few interactions on glucose transport was further tested directly using uptake assays. We observed that the glucose PTS components inhibit glucose transport through non-PTS glucose transporters.

III. Conclusions

Interactions of glucose PTS components with non-PTS transporters are influenced by the phosphorylation state of PTS components. Our results suggest that glucose, the most preferred sugar for *E.coli*, not only inhibits non-preferred sugars but also regulates its own uptake. We observed that glucose PTS inhibits glucose transport through the galactose transporters to make glucose transport more cost effective.

References

(1) DeutscherJ, Francke C, PostmaPW (2006) How phosphotransferase system related protein phosphorylation regulates carbohydrate metabolism in bacteria. *Microbiol.Mol Bio Rev* 70:939-1031

(2) Escalante, A., A. Salinas Cervantes, et al. (2012). "Current knowledge of the Escherichia coli phosphoenolpyruvate-carbohydrate phosphotransferase system: peculiarities of regulation and impact on growth and product formation." *Appl Microbiol Biotechnol* 94(6): 1483-1494