

From Textbook to Reality: How the Glucose Effect in lac Operon Regulation Really Works

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Abstract:

The lac operon in *E. coli* is the most commonly discussed example of gene regulation in genetics, microbiology, and molecular biology courses. It provides excellent examples of trans-acting regulatory proteins such as the lac repressor, cis-acting sequences such as the lac operon operators, the role of small molecules such as lactose as regulatory signals, and the use of genetic and biochemical experiments to understand gene regulation. All the textbooks I have checked do a very good job discussing the role of the lac repressor in the negative regulation of the lac operon. However, these same textbooks, and even most review articles in the scientific literature, do not reflect the current state of our research understanding of the so-called positive regulation or what I call “the glucose effect”. While the CRP/cAMP complex does help RNA Polymerase bind to the lac operon promoter, this is not the mechanism where glucose has its impact. It turns out that we have had data available as to the actual mechanism of the glucose effect since 1997, and nature’s reality is really cool! I will present the results from two papers (Inada et al., 1996, *Genes Cells* 1:293-301; Kimata et al., 1997, *Proc. Natl. Acad. Sci. USA* 94:12914-9) and show how I use one figure from the Kimata et al paper in my genetics course to walk students through a great set of experiments that leads them closer to nature’s truth.

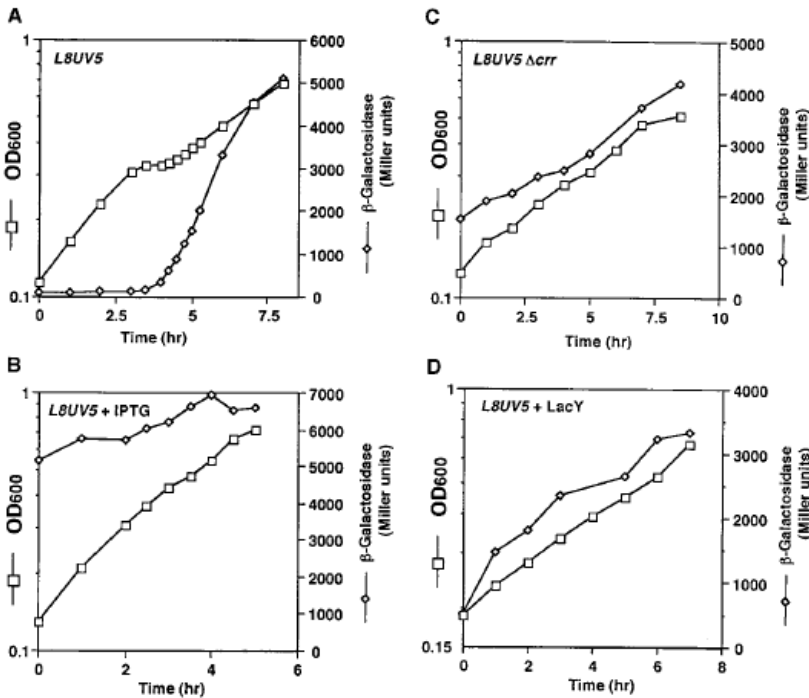


Figure 1 from Kimata et al., 1997

Basal state = L8UV5 double mutant
 L8 mutation abolished CRP binding site
 UV5 mutation improved lac operon promoter
 Basic growth curve in minimal media + glucose + lactose
 Squares denote OD600 measure of culture growth
 Circles denote beta-galactosidase enzyme activity

Panel A shows diauxic growth even when CRP is not helping RNA Polymerase bind to lac promoter, so CRP/cAMP is not mediating the glucose effect.

Panel B shows that IPTG abolishes the glucose effect even though lactose was in culture medium already, suggesting that lactose is not getting into cells right away.

Panel C shows that PTS glucose transporter (crr encodes the cytoplasmic component) is required for the glucose effect, suggesting that glucose transport somehow inhibits lactose transport.

Panel D shows that LacY permease is the target of the glucose effect.

Other data in Kimata et al., 1997 show that CRP is needed for expression of glucose transporter.

Follow up papers:

Hoischen et al., 1996, *J. Bacteriology* 178:6082-6
 Sondej et al., 1999, *Proc. Natl. Acad. Sci. USA* 96:3525–30

A different take on lac regulation, but very cool:

Eswarappa et al., 2009, *PLoS ONE* 4:e5789

Figure 1 from Sondej et al., 1999

Mutagenesis implicates 2 central cytoplasmic loops of LacY as binding targets for glucose transporter-mediated inhibition of lactose transport
 2 central loops of LacY share similarity with cytoplasmic loops of other membrane proteins that are inhibited by glucose transport

