Control analysis as a tool to understand the formation of the las operon in Lactococcus lactis

In Lactococcus lactis the enzymes phosphofructokinase (PFK), pyruvate kinase (PK) and lactate dehydrogenase (LDH) are uniquely encoded in the las operon and we here apply Metabolic Control Analysis to study the role of this organisation. Earlier work showed that LDH at wildtype level has zero control on glycolysis and growth rate but high negative control on formate production. We find that PFK and PK have zero control on glycolysis and growth rate at the wildtype enzyme level but both enzymes exert strong positive control on the glycolytic flux at reduced activities. PK has high positive control on formate and acetate production, whereas PFK has no control on these fluxes. Decreased expression of the entire las operon resulted in a strong decrease in growth rate and the glycolytic flux; at 53% expression of the las operon the glycolytic flux was reduced to 44% and the flux control coefficient increased towards 3. Increased las expression resulted in a slight decrease in the glycolytic flux. At the wildtype level the control was close to zero on both glycolysis and the pyruvate branches. The sum of control coefficients for the three enzymes individually was comparable to the control coefficient found for the entire operon; the strong positive control by PK almost cancels out the negative control by LDH on formate production. The analysis suggests that co-regulation of PFK and PK provides a very efficient way to regulate glycolysis, and co-regulating PK and LDH allows the cells to maintain homolactic fermentation during regulation of glycolysis.

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