Toetab TÜ ja TTÜ doktorikool
"Funktsionaalsed materjalid ja tehnoloogiad" (FMTDK)

ESF projekt 1.2.0401.09-0079

GROWTH RATE DEPENDENT DYNAMICS IN *LACTOCOCCUS LACTIS* METABOLISM STUDIED BY OMICS AND METABOLIC FLUX ANALYSIS

Petri-Jaan Lahtvee[1,2], *Kaarel Adamberg*[1,3], *Liisa Arike*[1,3], *Ranno Nahku*[1,2], *Kristo Abner*[1,2], *Raivo Vilu*[1,2]

[1]*Competence Centre of Food and Fermentation Technologies, Akadeemia tee 15b, Tallinn 12816, Estonia;*

[2]*Tallinn University of Technology, Department of Chemistry, Akadeemia tee 15, Tallinn 12816, Estonia;*

[3]*Tallinn University of Technology, Department of Food Processing, Ehitajate tee 5, Tallinn 19086, Estonia*

e-mail: petri@tftak.eu

Lactic acid bacteria is widely used in industry, however, its growth rate dependent metabolism is still poorly studied. A comprehensive study describing adaptive responses of *Lactococcus lactis* metabolism to the change of growth rate was characterized by the level of metabolic footprint (including consumption of amino acids), global transcriptome and proteome analysis. *L. lactis* was cultivated in strictly controlled glucose limited conditions on chemically defined medium using the accelerostat (A-stat) method in the specific growth rate range 0.1 – 0.6 h^{-1}. In addition to growth rate dependent metabolic switch point's determination, this cultivation method enabled to acquire steady state production and consumption yields of measured metabolites. Latter data was used to calculate intracellular fluxes using whole genome based metabolic flux analysis (MFA), containing 375 metabolites and 580 reactions.

Lactococcus lactis showed decreased consumption yields of amino acids during increase of specific growth rate until the value of 0.4 h^{-1}, where most of them levelled at their minimal values. Near the same switch point, formation of side products and energy wasting cycles (as shown by MFA) started to decrease, changing the metabolism into fully homolactic near maximal growth rate. Based on measurement of 2234 gene and 713 protein expression changes it was proposed, that carbon catabolite repression, regulated by carbon control protein-A, mediated shift from sugar transport towards amino acid transport may play an important role in latter metabolic shift. This was the first study, where correlation of transcriptome and proteome as well as growth rate dependent consumption patterns for all 20 amino acids in *L. lactis* were presented. It can be concluded that well reproducible A-stat approach compared to chemostat enables faster collection of massive amount quasi steady state data at defined environmental conditions, making it a suitable method for studying metabolic switch points in microorganisms' growth space.