

## DESCRIPTION OF GROWTH EFFICIENCY AND AMINO ACID METABOLISM IN *LACTOCOCCUS LACTIS* AT VARIOUS SPECIFIC GROWTH RATES AT SYSTEMS BIOLOGY LEVEL

<sup>a, b</sup> Petri-Jaan Lahtvee, <sup>a, c</sup> Kaarel Adamberg, <sup>a, b</sup> Kadri Aller, <sup>a, c</sup> Liisa Arike, <sup>a, b</sup> Ranno Nahku, <sup>a, b</sup> Raivo Vilu

<sup>a</sup> Competence Center of Food and Fermentation Technologies, Akadeemia tee 15b, Tallinn, Estonia; <sup>b</sup> Tallinn University of Technology, Institute of Chemistry, Akadeemia tee 15, Tallinn, Estonia; <sup>c</sup> Tallinn University of Technology, Institute of Food Technology, Ehitajate tee 4, Tallinn, Estonia

e-mail: petri@tftak.eu

*Lactococcus lactis* is recognised as a safe (GRAS) microorganism and has hence gained interest in numerous biotechnological approaches. As it is fastidious for several amino acids, optimization of processes which involve this organism requires a thorough understanding of its metabolic regulations during multisubstrate growth. Using glucose limited continuous cultivations, specific growth rate dependent metabolism of *L. lactis* including utilization of amino acids was studied based on extracellular metabolome, global transcriptome and proteome analysis. A new growth medium was designed with reduced amino acid concentrations to increase precision of amino acid consumption measurements. Consumption patterns were calculated for all 20 amino acids and measured carbon balance showed good fit of the data at all growth rates studied. It was observed that metabolism of *L. lactis* became more efficient with rising specific growth rate in the range 0.10 - 0.60 h<sup>-1</sup>, indicated by 30% increase in biomass yield based on glucose consumption, 50% increase in efficiency of nitrogen use for biomass synthesis, and 40% reduction in energy spilling. The latter was realized by decrease in the overall product formation and higher efficiency of incorporation of amino acids into biomass. *L. lactis* global transcriptome and proteome profiles showed good correlation supporting the general idea of transcription level control of bacterial metabolism. However, glycolysis and nucleotide synthesis showed more complex multilevel regulations. The current study demonstrates advantages of the usage of strictly controlled continuous cultivation methods combined with multi-omics approach for quantitative understanding of amino acid and energy metabolism of *L. lactis* which is a valuable new knowledge for development of balanced growth media, gene manipulations for desired product formation etc.



Toetab TÜ ja TTÜ doktorikool "Funktsionaalsed materjalid ja tehnoloogiad"(FMTDK) ESF projekt 1.2.0401.09-0079