Metabolic engineering of *E. coli* for the production of L-valine and its transcriptome/fluxome analysis

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We constructed L-valine production stain with Escherichia coli W3110 by targeted genetic modification and identified the effect of the biosynthesis of L-valine on cell physiology by combined transcriptome and fluxome analysis. The L-valine-producing strain was constructed by releasing two regulatory mechanisms, feedback inhibition and attenuation. Two amino acids alterations were introduced into *ilvH* which is subject to feedback inhibition by site-directed mutagenesis. The leader region of *ilvGMEDA* and *ilvBN* operon which is involved in attenuation was changed with the strong tac promoter by homologous recombination. Further improvement of the L-valine-producing strain was achieved by knocking out *leuA*, *panB* and *ilvA* thus making more substrate available for the L-valine biosynthesis. Combined transcriptome and fluxome analysis reveals that an increased pyruvate and ketoisovalerate availability is essential to direct the flux into the L-valine biosynthesis. Furthermore, target genes for further metabolic engineering can be selected from the combined analysis data. (This work was supported by Korean Systems Biology Research Grant, M10309020000-03B5002-00000 from the MOST.)