Influence of intracellular trehalose and Nε-lysine acetylation on protein aggregation in *Escherichia coli*

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Trehalose is a nonreducing disaccharide widely spread in nature which can serve as carbon reservoir, signalling molecule in the control of glucose metabolism and stress-protectant. It has been suggested that trehalose may stabilize proteins and prevent their aggregation. However, the mechanisms behind this protective function *in vivo* remain unclear. The findings presented in this doctoral dissertation expand our perception of the influence of trehalose on protein aggregation. This work shows that lack of intracellular trehalose synthesis in stationary-phase *E. coli* cells (Δ*otsA*) boosts N_{ε}-lysine acetylation of proteins which, in turn, can enhance their hydrophobicity and aggregation propensity. The aggregated proteome in stationary phase reflected the translation inhibition and the σ^S (RpoS)-stress response occurring in starved cells. Notably, the lack of intracellular trehalose enhanced the aggregation of EF-Tu and certain ribosomal proteins.

The link between Nε-lysine acetylation and protein aggregation was confirmed at the aid of *E. coli* strains impaired in their acetylation (Δ*ackA-pta*) and deacetylation (Δ*cobB*) pathways and extended to a recombinant protein model (VP1GFP). In general, decreased Nε-lysine acetylation reduced the formation of endogenous and recombinant protein aggregates, whereas increased Nε-lysine acetylation and decreased deacetylation enhanced aggregation.

These *in vivo* observations were experimentally validated with *in vitro* and *in silico* approaches, confirming the potential of Nε-lysine acetylation to generally modulate endogenous and recombinant protein aggregation in *E. coli* cells.