EFFECT OF OVER EXPRESSING PROTECTIVE ANTIGEN ON GLOBAL GENE TRANSCRIPTION IN BACILLUS ANTHRACIS BH500

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Protective antigen (PA) of *Bacillus anthracis* is being considered as a vaccine candidate against anthrax and its production has been explored in several heterologous host systems. Since the expression approaches tested, introduced adverse issues such as inclusion body formation and endotoxin contamination, the production from *B. anthracis* is presently considered as a preferred method. In this presentation we will report on the effect of protective antigen expression on the metabolism of the producing train *B. anthracis*, BH500, by comparing it with a control strain carrying an empty plasmid. The two strains were grown in a bioreactor and RNA-seq analysis of the producing and non-producing strain was performed. Several differences were observed, especially significant were the following: the strain expressing rPA showed increased transcription of *sigL,* the gene encoding RNA polymerase σ^{54}, *sigB*, the general stress transcription factor gene and its regulators *rsbW and rsbV*, as well as the global regulatory repressor *ctsR.* At the same time there were also decreased expression of intracellular heat stress related genes such as *groL, groES, hslO, dnaJ,* and *dnaK* and increased expression of extracellular chaperons *csaA* and *prsA2.* Additionally, major central metabolism genes belonging to TCA, glycolysis, PPP, and amino acids biosynthesis were up-regulated in the PA-producing strain which was associated with decreased specific growth rates. The information and the observation acquired from this study will be presented together with possible approaches to create a better producing strain.