MODULATION OF *E. COLI* AtoS-AtoC TWO COMPONENT SYSTEM BY BIOGENIC AMINES

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Antizyme (Az), known as a protein non-competitive inhibitor, induced by polyamines, the end product of enzymic reaction of ornithine decarboxylase. Az proved to be the *atoC* gene product, encoding the response regulator AtoC of the bacterial two-component signal transduction system AtoS-AtoC. The gene located just upstream of *atoC* encodes the sensor kinase, named AtoS. The biosynthesis of polyamines in the bacterial system is modulated posttranslational through the Az or at the transcriptional level by the induction of different genes. Upon acetoacetate induction, AtoS-AtoC system directly effects the *atoDAEB (ato)* operon transcription to regulate positively the biosynthesis of short-chain poly-(R)-3-hydroxybutyrate (cPHB) biosynthesis. Both AtoS and AtoC are necessary components for the positive transcriptional regulator of the *atoDAEB* operon genes.

Polyamines, which reported to induce AtoC in *E. coli*, activated the expression of *atoC* gene. A series of synthetic polyamine analogues have been tested for their effectiveness on the expression of *atoC*, as well as that of the *atoDAEB* operon. Putrescine and diaminopropane analogues, activated *atoC* transcription, indicative of the structural requirements of diamines for Az induction. In addition, this *atoC* induction resulted in accumulation of Az protein and inhibition of ODC activity due to formation of inactive ODC-Az complex.

Histamine down-regulated poly-(R)-3-hydroxybutyrate biosynthesis irrespective of the expression of the two-component system, whereas compound 48/80 up-regulated poly-(R)-3-hydroxybutyrate biosynthesis, maximal induction being obtained in the presence of multiple copies of the AtoS-AtoC two-component system. Interestingly, co-administration of histamine counteracted this inductive effect of compound 48/80 irrespective of the time course of its addition. Histamine was also tested for its effect on the activity of ODC and on the growth of polyamine-deficient *E. coli* cells. The reported data provide the first evidence for a differential modulator role

of histamine and compound 48/80 on the AtoS-AtoC two-component system signalling in potentially pathogenic bacteria, leading to a new perspective on their symbiotic behaviour.