[C1-4]

Upregulation of the Aldehyde Reductase by Constituvely Activating Mutations in the Transcriptional Regulator Confers *Escherichia coli* Resistance to Glyoxal

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The short chain carbohydrates such as glyoxal (GO) are generated *in vivo* from various sugars by oxidative stress, which are believed to be removed by the glutathione-dependent glyoxalase system. We isolated a number of glyoxal-resistant mutants from *E. coli* MG1655 strain on LB plate containing 8~10 mM glyoxal. By either tagging the mutations with transposon TnphoA132 or determining their cotransductional linkages, we were able to define a locus, in which most of the GO-resistant (GOR) mutations were mapped. DNA sequencing of the mutations revealed the mutated gene, presumably encoding an AraC-type transcriptional regulator of unknown function. The GO-resistant mutations result in missense or in-frame insertional changes of the gene, being localized in the putative regulatory domain. A likely target of this regulator was identified by the glyoxal-sensitive phenotype of an insertional inactivation of the next gene as well as a constitutive overproduction of its protein in GO-resistant mutant. The higher level of intracellular protein allows cells to enhance reduction of glycolaldehyde as detected by NMR, which was supported by an NADPH-dependent enzymatic activity. The glyoxal resistancy appears to be conferred by a two-step process involving aldo-keto reductase (AKR) and aldehyde reductase via glycolaldehyde intermediate. The AKR/aldehyde reductase regulatory circuit is one of few examples of metabolizing systems for C-2 carbohydrates characterized so far, which is likely to play a critical role in coupling oxidative stress and metabolism associated with sugars.