protein may have a direct contact with various nuclear receptors (e. g. T3, glucocorticoid receptors, retinoid receptors, ER (estrogen receptor)), with some signaling pathways (by the interaction of IL-1, and beta-catenin), also with other proteins such as p53 and p300. ADA3 protein was even found to be a target of HPV E6 oncoprotein. Presumably, ADA3 protein is a pivotal contributory partner in many gene expression regulatory processes and abnormal function and regulation of ADA3 may cause severe impairments, such as developmental disorders, or oncogenesis. Since our group's main area of interest is to gain insight into the relationship between histone modifications and tumors, ADA3 is a promising object of investigation.

Previously, the promoter sequence of the *Ada3* gene has been identified in *Drosophila melanogaster* (*dAda3*). On the basis of *in silico* analysis, some truncated promoter variants were produced. The functionality of these promoter fragments were comparatively examined in luciferase reporter gene expression assays, applied in S2 *Drosophila* embryonic cell culture. Using this approach, promoter segments were shown to affect the transcription of the reporter gene, both positively and negatively. Within these segments predicted binding sites were identified, which are dedicated to three well-known transcription factors, namely the *Hunchback*, *Hairy* and *Deformed*.

To describe the ontogenetic expression pattern of the *dAda3* in details, the mRNA level of this gene was measured by qPCR in 15 different developmental stages. The results show that the initial (maternal) amount of the Ada3 transcript is fairly decreased by the time of hatching. Both at the beginning and the end of the prepupa stage, definite increasing was observed, which both coincide with "ecdysone peaks" well-known from developmental biology of fruit fly.

Querying various databases, genes with spatiotemporal expression similar to *dAda3* were identified. According to high-throughput ChIP assays, within the upstream regions of these genes there are resembling TF binding patterns. Meta-analysis of public transcriptome datasets from NCBI GEO revealed numerous additional genes with *dAda3*-related expression. All these genes were used as a core of a predictive interaction network. Strikingly, beside physical and genetic relationships, the representation of GO terms clearly emphasize novel potential functions.

Our experimental results and the analysis of related bibliographic data suggest that *dAda3* has important roles in some fundamental mechanisms like cell cycle, gametogenesis, neuronal differentiation, oxidative stress response and ecdysone pathway. Although the exact mechanism of these interactions is not known, these predicted functions are expected to be conserved in a wide range of eukaryotic organisms. Thus, our subsequent research is planned to focus on a specific area of this subtle commitment.

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No evidence that bacterial gene regulation has adapted to mitigate the accumulation of toxic metabolites

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It has often been suggested that removal of toxic small molecules from the cell is necessary to the survival of the organism. In case of toxic intermediate metabolites, prevention of accumulation helps averting cellular damage. One potential strategy to achieve this is the tight regulation of producing and consuming enzymes around the damaging metabolite. In yeast, it has previously been suggested that toxic intermediate metabolites have their enzymatic genes clustered on the chromosome to promote such coregulation. However, a direct link between coregulation and metabolite toxicity remains unestablished. Here we focused on Escherichia coli to systematically test this theory by making use of a unique toxicity prediction algorithm that has been specifically designed for this organism. We tested two possible strategies to achieve tight coregulation for metabolic genes around toxic intermediates: co-regulation via shared regulators and allocation of genes within the same operon, a bacteria-specific mechanism of strong co-regulation. We show that while toxic intermediates have their neighbouring genes more often in the same operon than expected by chance, this effect is not general bur rather confined to few metabolic pathways. Furthermore, coregulation or mRNA-level coexpression of neighboring enzymes occur with similar frequency in case of both toxic and non-toxic intermediates. Taken together, even in an organism with huge population size, we failed to find any general signature of adaptation to specifically enhance co-regulation of genes participating in the production or consumption of toxic intermediate metabolites. These negative results could indicate that most potentially harmful metabolites do not reach toxic concentrations under physiological conditions. Alternatively, the lack of regulatory mechanisms to avoid toxic metabolite accumulation might be owing to suboptimal gene regulation, which appears to be widespread in bacteria.

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