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BACTERIAL PHYSIOLOGY

Unfit expression

CORBIS

> “detrimental genes were more highly expressed than other genes”

It is generally thought that bacteria regulate gene expression to adapt to changes in their environment. This implies that genes are expressed only when they are needed and are otherwise turned off to avoid producing proteins when they are not required or are toxic. A new study by Arkin and colleagues challenges this view of adaptive regulation of gene expression and shows that, instead, many genes do not respond appropriately to external clues.

An adaptively controlled gene is expected to be upregulated when it is essential for bacterial growth and thus provides a fitness benefit, and downregulated when it is not required and its expression has a fitness cost. To test this hypothesis, Arkin and colleagues cultured wild-type and transposon-mutant pools of the metal-reducing bacterium *Shewanella oneidensis* str. MR-1 in 15 different conditions, such as differing carbon sources, aerobic versus anaerobic growth or the presence of toxic compounds. They collected gene expression data for wild-type bacteria and assessed mutant fitness by using microarrays to calculate strain abundance. In total, they identified 1,172 different combinations of genes and conditions in which gene inactivation by a transposon insertion caused a mutant strain to grow better than the wild-type strain.

When the authors measured wild-type gene expression, they found that detrimental genes were more highly expressed than other genes in all conditions, indicating that genes with a fitness cost are not downregulated. About one-third of the detrimental genes were selfish elements such as transposases or prophages, or genes involved in motility, which might exhibit different effects in well-shaken laboratory cultures than in nature. The remaining two-thirds of detrimental genes showed inexplicably high expression and suboptimal adaptation of gene expression levels to culture conditions. Furthermore, there was only a weak correlation between relative gene expression and differential fitness in paired conditions. This means that genes which were important for fitness in one condition but not in another were not necessarily upregulated in the beneficial condition; in fact, some were even downregulated. Overall, only 5% of the examined *S. oneidensis* str. MR-1 genes showed adaptive regulation, whereas almost 50% showed suboptimal, non-adaptive control. Some of these genes are constitutively expressed or regulated by the cellular growth rate; for the rest, however, the regulatory mechanisms are less clear.

The ethanol-producing bacterium *Zymomonas mobilis* str. ZM4 and the sulphate-reducing bacterium *Desulfovibrio alaskensis* str. G20 also showed non-adaptive gene regulation. Both species failed to upregulate the metabolic genes needed to grow in minimal medium but not in rich medium. However, *Escherichia coli* str. K-12 showed adaptive regulation to minimal and rich media. The authors conclude that, under laboratory conditions, suboptimal, non-adaptive regulation of gene expression is widespread in bacteria. Although the mechanisms involved are unclear, they speculate that non-adaptive regulation reflects indirect control by factors that are not related to gene function.

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ORIGINAL RESEARCH PAPER Price, M. N. *et al.* Indirect and suboptimal control of gene expression is widespread in bacteria. *Mol Syst. Biol.* **9,** 660 (2013)