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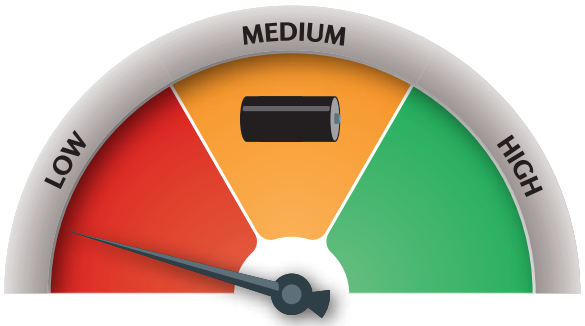

BACTERIAL PHYSIOLOGY

Persisters running out of energy

> ATP depletion … functions as a general mechanism for persister formation

Persisters are multidrug-tolerant cells in a bacterial population that have been linked to chronic infections. In *Escherichia coli* it was proposed that the stress response and the mRNA interferase toxin–antitoxins may contribute to the formation of persisters; specifically, during stress, increased levels of the alarmone guanosine tetraphosphate (ppGpp) promote the expression of toxins that, in turn, inhibit essential cellular functions such as translation, which leads to a dormant state.

Further examining the role of toxins in the formation of persisters, Shan *et al.* found that although the expression of mRNA interferase toxins was increased in *E. coli* under various stress conditions (including starvation, osmotic stress, pH stress and NaCl stress), persister formation was only observed when the bacterial stringent response was triggered following amino acid starvation. This finding suggests that the toxin–antitoxin system has a limited role in persister formation in these cells. Moreover, it was previously shown that during the stringent response, high levels of ppGpp not only activate mRNA interferases but also decrease rRNA synthesis by inhibiting the 16S rRNA promoter *rrnB* P1. However, the authors of this study showed that in *E. coli* repression of the *rrnB* P1 promoter led to the formation of persisters independently of both ppGpp and mRNA interferases, which suggests that another mechanism might have a role in persister formation.

The authors went on to show that decreased intracellular levels of ATP led to a decrease in *rrnB* P1 expression and increased persister formation. As antibiotics target ATP-dependent processes, such as protein synthesis, the authors suggest that intracellular ATP depletion lowers the antibiotic target activity and thus functions as a general mechanism for persister formation.

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ORIGINAL ARTICLE Shan, Y. *et al.* ATP-dependent persister formation in *Escherichia coli*. *mBio* **8**, e02267-16 (2017)