BACTERIAL PHYSIOLOGY

Stressed bacteria aren't lost without a leader

IMAGE SOURCE

Toxin–antitoxin (TA) modules consist of a stable toxin and a labile antitoxin and are used to regulate growth and death in bacteria in response to a variety of signals. Vesper *et al.* now describe how MazF can specifically upregulate the expression of a subset of cellular proteins against a background of protein synthesis shutdown.

The MazEF system is one of the best characterized TA modules in

Escherichia coli. Stress conditions result in degradation of MazE, the labile antitoxin, and release of MazF, a sequence-specific endoribonuclease toxin that preferentially targets ACA sequences in single-stranded mRNAs, thereby inhibiting protein synthesis. It was shown previously that this inhibition was incomplete and that MazF induction actually results in the specific synthesis of approximately 10% of cellular proteins, despite the fact that the mRNAs encoding many of these proteins contain ACA sequences. To investigate this phenomenon further, Vesper *et al.* induced the expression of MazF in *E. coli* and used primer extension to map the termini of several of the upregulated transcripts. They observed that MazF induction resulted in cleavage of these transcripts at ACA sequences immediately upstream of the start codon, producing leaderless mRNAs (lmRNAs). The authors then pulse-labelled cells overexpressing MazF and observed the selective expression of a leaderless reporter gene, indicating that the lmRNAs are translated in the presence of MazF.

So how does MazF induction result in the specific upregulation of lmRNAs? 16S ribosomal RNA contains numerous ACA sequences, two of which may be accessible for cleavage by MazF. The authors incubated 70S ribosomes with purified MazF and observed ACA cleavage at a site that corresponds to position 1,500 in the 16S rRNA. This resulted in the removal of 43 nucleotides

from the 16S rRNA 3' terminus, the region that contains the anti-Shine–Dalgarno sequence, which interacts with the 5' leader and is required for translation initiation of canonical mRNAs. The authors confirmed that MazF cleaved the 16S rRNA *in vivo* and found that uncleaved 70S ribosomes were proficient for *in vitro* translation of both canonical mRNAs and lmRNAs, whereas MazF-cleaved ribosomes were only able to translate lmRNAs. Finally, the authors confirmed that 16S rRNA cleavage and lmRNA production occurred in cells in which MazF was induced by physiologically relevant stress signals.

Taken together, these data indicate that under cellular stress conditions, in addition to causing a general shutdown of protein synthesis, the toxin MazF upregulates expression of a subset of cellular proteins by creating a pool of lmRNAs and a subpopulation of 'stress ribosomes' to selectively translate them. The synthesis of these proteins is thought to contribute to the death of most of the population and the survival of a small subpopulation of cells under stress conditions.

Andrew Jermy

ORIGINAL RESEARCH PAPER Vesper, O. *et al.*

Selective translation of leaderless mRNAs by specialized ribosomes generated by MazF in *Escherichia coli*. *Cell* **147**, 147–157 (2011)

FURTHER READING Amitai, S. *et al.* *Escherichia coli* MazF leads to simultaneous selective synthesis of both "death proteins" and "survival proteins". *PLoS Genet.* **5**, e1000390 (2009) | Yamaguchi, Y. & Inouye, M. Regulation of growth and death in *Escherichia coli* by toxin–antitoxin systems. *Nature Rev. Microbiol.* **9**, 779–790 (2011)