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BACTERIAL PHYSIOLOGY

New shears for SsrA

Stalled ribosomes are a problem for a cell: they deplete the pool of available ribosomes and lead to the formation of truncated proteins. Such ribosomes are rescued by SsrA (also called tmRNA), an RNA with properties of both tRNA and mRNA, which adds a small tag to incompletely synthesized proteins and targets them for degradation. Gur and Sauer report in a recent issue of the *Proceedings of the National Academy of Sciences USA* on an evolutionary twist in the evolution of SsrA.

When a ribosome becomes stalled on an mRNA, alanine-charged SsrA binds the unoccupied ribosomal A site. The alanine residue is added to the nascent peptide and the mRNA is replaced by part of SsrA. The ribosome then continues the translation of SsrA, which adds a short stretch of amino acids to the nascent peptide. This sequence is normally recognized by the ClpXP protease. This process rescues stalled ribosomes and removes incomplete proteins by targeting them for degradation.

SsrA is conserved in all bacteria sequenced so far, but what happens when a bacterium does not have ClpXP? Gur and Sauer investigated SsrA-mediated protein degradation in *Mycoplasma* spp., which lack many common proteases, and found that these organisms have recruited a different protease, Lon, to degrade proteins tagged by SsrA. The tag added by the SsrA of *Mycoplasma florum* is different from that of other Gram-negative and Gram-positive bacteria. Using *in vitro* degradation of peptide substrates, the authors identified the crucial residues in the tag that are recognized by Lon.

Proteins with the *M. florum* SsrA tag were efficiently degraded by *M. florum* Lon, but much less so by *Escherichia coli* Lon. Furthermore, *M. florum lon* could not complement an *E. coli lon* mutant. *In vitro* studies revealed that *M. florum* Lon rapidly degraded even stably folded proteins with the *M. florum* SsrA tag but not proteins with the *E. coli* SsrA tag.

The authors speculate that after *Mycoplasma* spp. lost ClpXP, evolutionary pressures selected for modified SsrA sequences that enabled recognition by Lon. This finding opens up new avenues for the *in vitro* study of Lon. Many natural Lon substrates are poorly soluble, but the addition of the *M. florum* SsrA tag to any protein can now produce a Lon substrate.

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> “…SsrA…adds a small tag to incompletely synthesized proteins and targets them for degradation.”

ORIGINAL RESEARCH PAPER Gur, E. & Sauer, R. T. Evolution of the ssrA degradation tag in *Mycoplasma*: specificity switch to a different protease. *Proc. Natl Acad. Sci. USA* **42**, 16113–16118 (2008)