GENE REGULATION

In charge of translation

The speed of ribosome progression has important consequences: for example, it can affect protein folding and translational accuracy. Codon usage has generally been considered as the main factor affecting ribosomal velocity, but this theory is challenged by a recent study that reveals a crucial role for positively charged amino acids.

Charneski and Hurst used ribosome profiling to study factors that affect ribosomal velocity in yeast. Such factors can be identified by assuming that mRNA regions that are slowly transcribed are more likely to have a ribosome bound to them.

First, the authors examined the effects of codon usage. The theory is that ribosomes slow down on encountering a codon that corresponds to a rare tRNA as they have to wait for the tRNA to be delivered. However, Charneski and Hurst found that codon usage explains little of the variation in ribosomal velocity. Similar conclusions were drawn for structures

predicted to cause mRNA folding, which have also been suggested to influence ribosome speed.

Instead, the authors find evidence for an alternative scenario in which positively charged amino acids in nascent proteins slow down translation owing to interactions with the exit tunnel of the ribosome. They show that positively charged residues greatly reduce ribosomal velocity and do so additively, such that the number of bound ribosomes correlates with the number of positively charged

residues. Overall, a large proportion of the variability in ribosomal velocity is explained by the number of positively charged residues.

These findings have wide implications, from understanding mechanisms of disease to designing transgenes that are efficiently expressed.

Louisa Flintoft

ORIGINAL RESEARCH PAPER Charneski, C. A. & Hurst, L. D. Positively charged residues are the major determinants of ribosomal velocity. *PLoS Biol.* **11**, e1001508(2013)