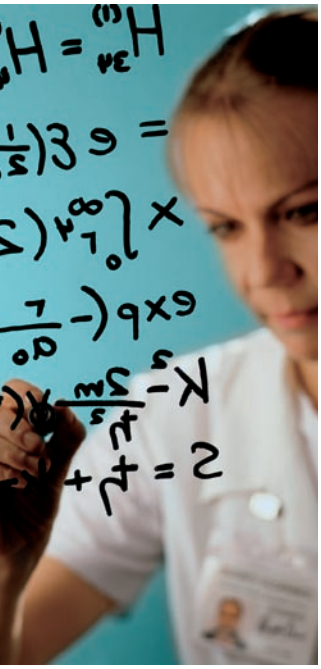
GENE EXPRESSION

Decoding translation



Translation of eukaryotic mRNAs depends on polyadenylation, but what determines exactly when and at what level individual mRNAs are translated? A new study shows how to read the code of sequence elements in the 3′ UTR that controls translation.

Translational activation by cytoplasmic polyadenylation depends on two elements in the 3′ UTR: the hexanucleotide AAUAAA site (Hex) and the cytoplasmic polyadenylation element (CPE), which is often present in several copies and is also necessary for translational repression. The Pumilio-binding element (PBE) is also thought to have a role in repression.

The authors used the cyclin B mRNAs of *Xenopus laevis* to work out how different arrangements of these elements determine whether an mRNA is repressed or activated, and whether it is activated early or late in the cell cycle. By attaching the 3′ UTRs of the five cyclin B mRNAs (B1–B5), along with various mutant derivatives, to a reporter construct and then measuring the translation and recruitment of *trans*-acting factors, they show that at least two CPEs were necessary for repression, with 10–12 nucleotides being the optimal distance between them. By contrast, activation required just one CPE, and its efficiency was determined by the distance between the CPE and the Hex, with 25 nucleotides being optimal. The contribution of the PBE was more subtle, affecting the activation efficiency of only some CPEs. The timing of activation depended on the extent of overlap between the Hex and one of the CPEs.

To test the code that the authors derived from these results, they scanned the 3′ UTRs in the *X. laevis*, mouse and human genomes for the different arrangements of elements and selected 27 conserved 3′ UTRs at random for validation. In approximately 90% of cases the activation and repression behaviours were as predicted by the code. The results of these predictions suggest that up to 20% of the genome might be subjected to this kind of regulation. Refinement of the code to account for additional elements, and testing the code across vertebrate genomes, will be the next step.

Patrick Goymer

ORIGINAL RESEARCH PAPER Piqué, M., López, J. M., Foissac, S., Guigó, R. & Méndez, R. A combinatorial code for CPE-mediated translational control. *Cell* **132**, 434–448 (2008)