A rare codon-based translational program of cell proliferation

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 4596341
Author(s) Guimaraes, Joao C.; Mittal, Nitish; Gnann, Alexandra; Jedlinski, Dominik; Riba, Andrea; Buczak, Katarzyna; Schmidt, Alexander; Zavolan, Mihaela
Author(s) at UniBasel Zavolan, Mihaela ; Azevedo Salgado Guimaraes, Joao Carlos ; Mittal, Nitish ; Gnann, Alexandra ; Jedlinski, Dominik ; Riba, Andrea ; Buczak, Katarzyna ; Schmidt, Alexander ;
Year 2020
Title A rare codon-based translational program of cell proliferation
Journal Genome Biology
Volume 21
Number 1
Pages / **Article-Number** 44
Keywords Cell proliferation; Codon usage; Rare codons; Translation control; Translation elongation; tRNA pools
Mesh terms Animals; Cell Proliferation, genetics; Codon Usage; Mice; NIH 3T3 Cells; Peptide Chain Elongation, Translational; RNA, Messenger, metabolism; RNA, Transfer, metabolism
The speed of translation elongation is primarily determined by the abundance of tRNAs. Thus, the codon usage influences the rate with which individual mRNAs are translated. As the nature of tRNA pools and modifications can vary across biological conditions, codon elongation rates may also vary, leading to fluctuations in the protein production from individual mRNAs. Although it has been observed that functionally related mRNAs exhibit similar codon usage, presumably to provide an effective way to coordinate expression of multiple proteins, experimental evidence for codon-mediated translation efficiency modulation of functionally related mRNAs in specific conditions is scarce and the associated mechanisms are still debated.; Here, we reveal that mRNAs whose expression increases during cell proliferation are enriched in rare codons, poorly adapted to tRNA pools. Ribosome occupancy profiling and proteomics measurements show that upon increased cell proliferation, transcripts enriched in rare codons undergo a higher translation boost than transcripts with common codons. Re-coding of a fluorescent reporter with rare codons increased protein output by 30% relative to a reporter re-coded with common codons. Although the translation capacity of proliferating cells was higher compared to resting cells, we did not find evidence for the regulation of individual tRNAs. Among the models that were proposed so far to account for codon-mediated translational regulation upon changing conditions, the one that seems most consistent with our data involves a global upregulation of ready-to-translate tRNAs, which we show can lead to a higher increase in the elongation velocity at rare codons compared to common codons.; We propose that the alleviation of translation bottlenecks in rapidly dividing cells enables preferential upregulation of pro-proliferation proteins, encoded by mRNAs that are enriched in rare codons.
Publisher BioMed Central
ISSN/ISBN 1474-7596 ; 1474-760X
edoc-URL https://edoc.unibas.ch/76093/
Full Text on edoc Available;
Digital Object Identifier DOI 10.1186/s13059-020-1943-5
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/32102681
ISI-Number WOS:000517487400001

Document type (ISI) Journal Article