Large-scale proteomics: The secrets of the secretory proteome

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Abstract

The amount of energy that cells invest in protein production is very high. The expression levels of proteins in living cells are derived from mass spectrometry (MS), GFP tagged proteins, antibody staining and ribosomal profiling. The tRNA Adaptation Index (tAI) is an indirect sequence-based measure that approximates the translation elongation efficiency. It considers the abundance of the relevant tRNAs and the codon–anticodon rules. Specifically, low and high tAI values indicate lower and higher translation rates, respectively.

We found that proteins that are rarely seen by MS tend to have low values of tAI. A non-uniform tAI values along the transcript implies pausing of the ribosome on certain codons, which affect the overall speed and effectiveness of translation. In all eukaryotes about a third of the proteins are translated by ribosomes that are docked at the ER membranes. These proteins include the membranous and the secretory proteins. A common feature of all secretory proteins is the signal peptide (SP) at the N'-terminus region. Previous studies showed lower tAI values at the initial segment of coding sequences of a wide range of organisms. We found that most of the cytosolic and membranous proteins do not display this trend. In contrast, proteins with a low tAI at the N'-terminal signify the secreted proteins that contain SPs. Overall, these proteins have a higher global tAI and are shorter in length. We conclude that the tAI profile is a reflection of an evolutional refinement of the secreted proteins whose translation must be tightly controlled. We postulate that the low tAI value at the initial segment attenuates translation and ensures the time necessary for SP cleavage while minimizing the effect of ribosomes' drop-off. We show that the hidden code for the secretory proteomes can be generalized to GPI-anchored proteins and mitochondrial proteins with transit sequences.