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A BIOINFORMATIC PIPELINE FOR STUDYING RIBOSOME OCCUPANCY IN CHO CELLS

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Translation is a central process in which protein is synthesized by ribosomes. The ribosomal profiling technique directly measures protein synthesis with resolution ranges from codon level to genome scale. Furthermore, it builds a bridge to fill in the gap between the transcriptome and proteome. Here we have developed a bioinformatic pipeline to analyze the ribosomal occupancy in Chinese hamster ovary (CHO) cells, and demonstrate its application to a CHO cell line that produces IgG. The pipeline quantifies ribosomal occupancy at each base pair of the genome. When analyzed with RNA-Seq levels, an assessment of ribosomal occupancy can be made, and correlated with codon usage, RNA structure, and other features to identify features that influence translation in CHO. We applied this to an IgG-producing CHO cell line growing exponentially and cells entering stationary phase. First, the pipeline allows us to quantify the distribution of 'translational power' at both time points, and compared the translation of the recombinant protein to host cell proteins (HCPs), including HCPs predicted by signalP to be secreted. Second, we are able to assess the influence of several features on ribosomal pausing, such as codon usage, signal peptides, and RNA structure. For example, we can identify how different amino acids influence translational pausing. This pipeline allows us to elucidate the cell processes and sequence-level features that influence recombinant protein translation in CHO cells, thus aiding in the design and engineering of this valuable protein expression host.