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*The alternative human proteome*

It has recently been hypothesized that alternative translation initiation of eukaryotic mRNAs might be used as a method to expand the proteome (Kochetov, A.V. 2008 Alternative translation start sites and hidden coding potential of eukaryotic mRNAs. *Bioessays*. 30, 683-91). Based on the idea that a single mRNA can produce three completely independent amino acid sequences if read in all three possible reading frames, this hypothesis suggests that the complexity of the eukaryotic proteome is largely underestimated. Several examples of out-of-frame alternative translation initiation in eukaryotes exist to support this hypothesis. However, almost all of these examples occur at an upstream AUG codon in relation to the +1 position of the main open reading frame (ORF). These alternative AUG codons are usually situated within an optimal Kozak context. Although extremely rare, a small number of examples of out-of-frame alternative translation initiation at a downstream AUG codon in an optimal Kozak context exist in mammals (Vanderperre et al. 2011 An overlapping reading frame in the PRNP gene encodes a novel polypeptide distinct from the prion protein. *FASEB J* 1793, 335-45).

Upon re-examination of the human genome, we found more than 10,000 predicted ORFs whose initiator codon is surrounded by an optimal Kozak context. In this project, we select some predicted ORFs and determine if the proteins are expressed. The findings will have direct implications regarding the comprehension of the physiological function of the human genome.

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