

PRESENCE OF UPATGS IN THE 5' UT REGION OF GENES OF MRNA: POTENTIAL IMPLICATIONS IN THE REGULATION OF GENE EXPRESSION AT TRANSLATIONAL LEVEL

CS Argolo¹, LL Loguercio¹

¹Universidade Estadual de Santa Cruz

Understanding major underlying mechanisms of regulating gene expression in fungi is relevant, due to several applications in agriculture and industry. Influence of mRNAs untranslated regions (UTRs) in this regulation has been recognized. The presence of AUGs upstream to the start codon of the mRNA (*upATGs*), originate small 5' open-reading frames (5' *uORFs*), which attenuate the translation rates of certain proteins through competition by the ribosomes. So far, little has been studied about the ubiquity of this mechanism in the genes of genomes. A specialized database, the 'UTRdb', has been devised to store information about these regions of mRNAs. Based on the availability of this resource, we sought to answer how representative this mechanism might be for gene regulation in fungi.

All UT sequences of mRNAs available for fungal species in the UTRdb were collected in the 'RefSeq' and the percentage of genes annotated to the respective genomes that are part of this database was verified. Most of the 15 fungal species found in UTRdb showed only 8-25% of their genomic genes represented in this database. Of these, 18-50% of 5' *uORFs* were found among the 5' UTRs. This indicates that analyses on the 5' *uORFs* in genomes are limited by the representativeness of genes in UTRdb. However, *Cryptococcus neoformans* and *Penicillium marneffeii* showed 65 and 43%, respectively, of their genomic genes in the UTRdb, with 25 and 50% of these genes containing potential 5' *uORFs*. Due to this higher representativeness, these species were chosen for further analysis. A survey of the stop codons associated with each *upATG* allowed us to assess the extent (in bp) of the 5' *uORFs* potentially formed, and classify them according to whether their stop codon were upstream or downstream to the real mRNA start codon. These parameters allow one to infer levels of potential interference of these 5' *uORFs* in translational regulation of their mRNAs. In both *C. neoformans* and *P. marneffeii*, greater than 80% of 5' *uORFs* revealed stop codons upstream of the mRNA's ATG.

The *uORFs* of *C. neoformans* have shown high potential to interfere with the translation of proteins predicted by the respective mRNAs, not only by the location of the 5' *uORFs* stop codons (mostly after the mRNA's ATG), but also by the presence of 5' *upATGs* with translation initiation contexts equal or stronger to that of mRNA's ATG, based on previous reports. In both cases, there is a strong tendency of the ribosomal machinery to be partially sequestered by the 5' *uORFs*, leading to spurious translations in the 5' UT region. Taken together, the results suggest that translation of several mRNAs in fungi is subject to translational regulation of gene expression, as an effect of the presence of 5' *uORFs*. These would lessen the rate of mRNA translation by competing for the translation initiation complex. Other studies are underway to determine whether this regulatory phenomenon is functionally scattered throughout the genome, or if there are groups of genes (with specific functions) that preferentially depend on this form of gene regulation.

Supported by: ICB/UESC.