BDR SEMINAR in Yokohama

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13:30-14:30, C210-212, Yokohama Central Research Building

Control of non-AUG codon translation by eIF5-mimic protein

Summary

Translation initiation from non-AUG codons plays important roles in various gene regulation programs. In bacteria, GUG initiation is an integral part of an RNA switch regulating replication protein of plasmids. GUG or UUG initiation is permitted in part by a simpler set of initiation factors than those found in eukaryotes. However, in eukaryotes, initiation is more accurate, repressing most events of non-AUG initiation to a very low level. Here we show that the non-AUG initiation rate is nearly consistent under a fixed context in various human and insect cells. Yet, it ranges from <1% to nearly 100% compared to AUG translation, depending on Kozak and other new nucleotide contexts. Mechanistically, this range of non-AUG initiation is controlled in part, by the eIF5-mimic protein (5MP). 5MP represses non-AUG translation by competing with eIF5 for the Met-tRNAi-binding factor eIF2. Thus, eIF5 increases and 5MP decreases translation of *NAT1/EIF4G2/DAP5* whose sole start codon is GUG. Using eIF5 and 5MP1 as tools, ribosome profiling identifies a handful of new non-AUG initiation sites, some of which serve as sole start codons. We propose that the homeostasis of non-AUG translatome is maintained through balanced expression of eIF5 and 5MP. We discuss the significance of this finding in the biology of cancer and infectious diseases.

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