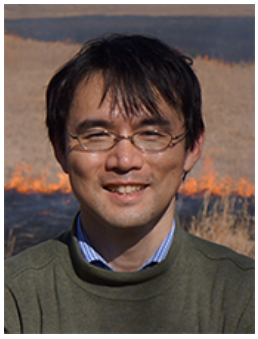
Seminar

Translational recoding by RNA chemical modification of non-AUG start codons



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In contrast to prokaryotes wherein GUG and UUG are permissive start codons, CUG is considered as the strongest non-AUG start codon in most eukaryotes. Post-transcriptional and translational control by RNA chemical modifications is the subject of extensive research, with COVID pandemic and the emergence of mRNA vaccines. Of note, the Pferser Biontech SARS-CoV2 mRNA vaccine Comirnaty replaces uridines with 1N-pseudouridine (1N-Ψ) as the latter is believed to avoid innate immunity against RNAs. Here, we report that combined 5-cytosine methylation (5mC) and pseudouridylation (Ψ) of near-cognate non-AUG start codons convert GUG and UUG initiation favored over CUG initiation in eukaryotic translation. This prokaryotic-like preference is attributed to enhanced NUG initiation by Ψ in the second base, and reduced CUG initiation by 5mC in the first base. Molecular dynamics simulation of $tRNA_i^{Met}$ anticodon base-pairing to the modified codons demonstrates that these modifications directly alter the affinity of codon:anticodon pairing within the ribosomal pre-initiation complex, thereby modulating the efficiency of initiation from the modified codons. Modulation of translation by 5mC and Ψ introduced to non-AUG start codons can offer a new layer of control of eukaryotic proteome diversity as well as technical repertoire to generate synthetic RNA tools.

2021

7/28(Wed)

15:00～16:30

E131, Build E

Those who wish to attend the seminar online need to register via Google Form https://forms.gle/H4NTYnky8oo4ykCt8 at least one day before the seminar. Teams URL will be sent to registrants. For inquiries, please contact Yasushi Yoshioka @ yoshioka@bio.nagoya-u.ac.jp, ext 2537.

GTR seminar / Topics in Advance Biological Science