Different mechanism of reading the isoleucine codon in three domains of life

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Transfer RNAs (tRNAs) read codons of mRNA as a triplet and converts the message from nucleic acid to proteins. The universal genetic code consists of 64 triplets of which 61 represent different amino acids. The number of tRNA species is always fewer than the 61 codons suggesting that some tRNAs must read more than one codon. This ability is due to the wobble hypothesis where base 34 of tRNA can pair with multiple bases. Isoleucine is the only amino acid which is represented by 3 codons AUC, AUU and AUA. There are different mechanisms of reading the AUA codon in eukaryotes and bacteria. Eukaryotes contain a tRNAIle with the anticodon ΨAΨ (Ψ=pseudouridine) which preferably read the isoleucine codon AUA. Bacteria use a tRNAIle with the anticodon LAU (L=lysidine). Lysidine is a modified cytidine in which the wobble base cytidine is chemically modified by amino acid lysine. Using biochemical and mass spectrometric analysis, we found that archaea uses agmatine (decaroxylated arginine) modified cytidine wobble base to read the codon AUA. The modification is known as agmatidine and it is very similar to lysidine. This modification prevents global mistranslation as the modified tRNA reads only the AUA codon without reading the AUG codon of methionone. The enzymes responsible for this modification are very similar in their function but different in structure indicating that they have evolved through convergent evolution. Essentiality of these modification enzymes and their absence in eukaryotes make them attractive drug targets.

Biography
Debabrata Mandal has completed his PhD from Bose Institute, India. He has completed his Postdoctoral studies from Department of Biology at Massachusetts Institute of Technology, USA. He is currently an Assistant Professor at National Institute of Pharmaceutical Education and Research-Hajipur, India. His research group is currently working on novel drug targets and their underlying mechanism in anti-leishmanial therapy.

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