

Supplementary information S1 (table) | Genetic code flexibility in microorganisms

Organisms and organelles	Mechanism	References
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**Biased codon usage**

Synonymous codons	Most sequenced organisms	Mutational bias or natural selection	<sup>1</sup>
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**Codon reassignment**

AUA: Ile→Met	Mitochondria of most metazoa and yeasts	Loss of tRNA <sup>Ile</sup> <sub>CAU</sub> and f <sup>b</sup> C modification of tRNA <sup>Met</sup> <sub>CAU</sub>	<sup>2</sup>
CUN <sup>a</sup> : Leu→Thr	Mitochondria of <i>Saccharomyces</i> spp.	Loss of tRNA <sup>Leu</sup> <sub>UAG</sub> ; evolution of tRNA <sup>Thr</sup> <sub>CAU</sub> from tRNA <sup>His</sup>	<sup>3,4</sup>
CUA/CUU: Leu→Ala	Mitochondria of <i>Ashbya gossypii</i>	Loss of tRNA <sup>Leu</sup> <sub>UAG</sub> ; evolution of tRNA <sup>Ala</sup> <sub>CAU</sub>	<sup>5</sup>
UAG: Stop→Ala	Mitochondria of certain green algae	Unknown	<sup>6</sup>
UAG: Stop→Leu	Mitochondria of certain green algae	Evolution of tRNA <sup>Leu</sup> <sub>CUA</sub>	<sup>6,7</sup>
UAG: Stop→Pyl	<b>Archaea</b> Methanoscincinales Methanomassiliicoccales <b>Bacteria</b> <i>Clostridia</i> Peptococcaceae, Halobacteroidaceae, Thermoanaerobacteraceae, Ruminococcaceae <b>Negativicutes</b> Sporomusa, unclassified <b>δ-Proteobacteria</b> Desulfospira, Bilophila, unclassified	Evolution of tRNA <sup>Pyl</sup> <sub>CUA</sub> , pyrrolysyl-tRNA synthetase, and pyrrolysine biosynthesis genes <i>pylBCD</i> . Normally occurs as a gene cassette ( <i>pylTSBCD</i> ).	<sup>8-10</sup>
UAR <sup>b</sup> : Stop→Gln	Certain green algae and phages	Evolution of tRNA <sup>Gln</sup> with UUA and CUA anticodons	<sup>11</sup>
UCA: Ser→Stop	Mitochondria of <i>Scenedesmus</i>	Loss of tRNA <sup>Ser</sup> <sub>UGA</sub>	<sup>12,13</sup>
UGA: Stop→Gly	SR1 bacteria, Gracilibacteria (ACD78, ACD80)	Evolution of tRNA <sup>Gly</sup> <sub>UCA</sub> divergent D-arm and anticodon stem	<sup>14</sup>
UGA: Stop→Cys	<i>Euploites</i> spp.	Evolution of tRNA <sup>Cys</sup> <sub>UCA</sub> ; eRF1 does not recognize UGA	<sup>15,16</sup>
UGA: Stop→Trp	Certain Firmicutes; mitochondria of most eukaryotic microorganisms	Mutation of tRNA <sup>Irp</sup> <sub>CCA</sub> to tRNA <sup>Irp</sup> <sub>CUA</sub> or C-to-U editing of tRNA <sup>Trp</sup> <sub>CCA</sub>	<sup>2,17,18</sup>

**Codon recoding**

Recoded UGA: Stop→Sec	<b>Bacteria</b> Found in certain species from the phyla: Firmicutes, Proteobacteria, Acidobacteria, Aquificae, Chloroflexi, Spirochaetes, Actinobacteria  <b>Archaea</b> Restricted to: <i>Methanopyrus kandleri</i> , Methanococcales  <b>Eukarya</b> In most clades excluding higher plants and fungi.	Particular UGA codons are recoded by downstream adjacent SECIS (in bacteria and archaea) or SECIS in 3'UTR (eukaryotes).  Requires tRNA <sup>Sec</sup> <sub>UCA</sub> , selenophosphate synthase ( <i>seID</i> ), Sec elongation factor ( <i>seIB</i> or EF-Sec), and Sec synthase ( <i>seIA</i> ) in bacteria or phosphoseryl-tRNA <sup>Sec</sup> kinase (PSTK) and Sep-tRNA <sup>Sec</sup> :Sec-tRNA <sup>Sec</sup> synthase (SepSecS) in archaea and eukaryotes.	19-22
Recoded UGA: Cys→Sec	<i>Euplates</i> spp.	SECIS elements in the 3'UTR recode certain UGA=Cys codons to Sec	15

**Ambiguous decoding**

ACN: Thr and Ser	<i>Escherichia coli</i> , <i>Mycoplasma</i> and likely other bacteria; yeast mitochondria	Loss of ThrRS editing due to oxidative stress or mutations	23-25
CUG: Leu and Ser	<i>Candida</i> and Ascomycetes	tRNA with CAG anticodon recognized by both leucyl- and seryl-tRNA synthetases	26-28
CUN, UUA, UUG: Leu, Ile, and Val	<i>Mycoplasma</i>	Loss of LeuRS editing	24
UUC, UUU: Phe, Tyr	<i>Mycoplasma</i> ; yeast mitochondria	Loss of PheRS editing	29
Mistranslation at all codons	Most microorganisms	Reduced ribosomal fidelity due to mutations, antibiotics, or starvation	30

<sup>a</sup> N=A, U, G or C<sup>b</sup> R=A or G

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