MS05 Nucleic acids and their interaction

MS5-01
The interactions between Guanine and Uracil
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Abstract
Decoding during ribosomal translation occurs through complex and interdependent molecular recognition networks between mRNA, tRNAs, and rRNAs. Among those, the stability of codon-anticodon triplets, the fold of the tRNA anticodon hairpin, the modified nucleotides, and the interactions with rRNA bases at the decoding site constitute key contributors. Based on biochemical and genetic data in the literature, coupled with many crystal structures of fully active ribosomes, nucleotide modifications in the anticodon loop are better understood molecularly. They contribute to the pre-organization of the anticodon loop with helicoidal stacking of the anticodon triplet (34-35-36) for efficient recognition and binding to the complementary mRNA triplet (3-2-1). The structures demonstrated that the ribosomal grip grasps the geometry and the steric volumes of the triplet pairs. Thus, at the first and second positions of the mini helix, the geometrical constraints imposed by the ribosomal grip at the decoding site stabilize a keto-enol tautomeric shift, either of the G or the U, in a GoU pair leading to a Watson-Crick-like configuration, isosteric to G=C or A-U pairs. Such near-cognate interactions are at the source of the most frequent translational errors observed. At the third position, GoU wobbles are expected. However, three forms are observed: the standard GoU with the U in the major groove, a new GoU* pair with U* in the minor groove, and the tautomeric Watson-Crick-like GoU or GoU*. The first two types are isosteric between themselves (G34oU3 occupies the same volume than U34*oG3). The last two types require base modifications in an asymmetric fashion: when the U is on the tRNA (U34) a modification is necessary (forming G3oU34*) but with G on the tRNA it is not necessary but can occur (forming U3oG34). In summary, the first two isosteric wobble GoU configurations are necessary to satisfy the wobbling rules for proper decoding, while the last tautomeric Watson-Crick-like configuration leads to translational errors. It is striking how molecular biology exploits the full physico-chemical spectrum of the keto bases G and U during the central process of translation for both controlling fidelity and accommodating errors.

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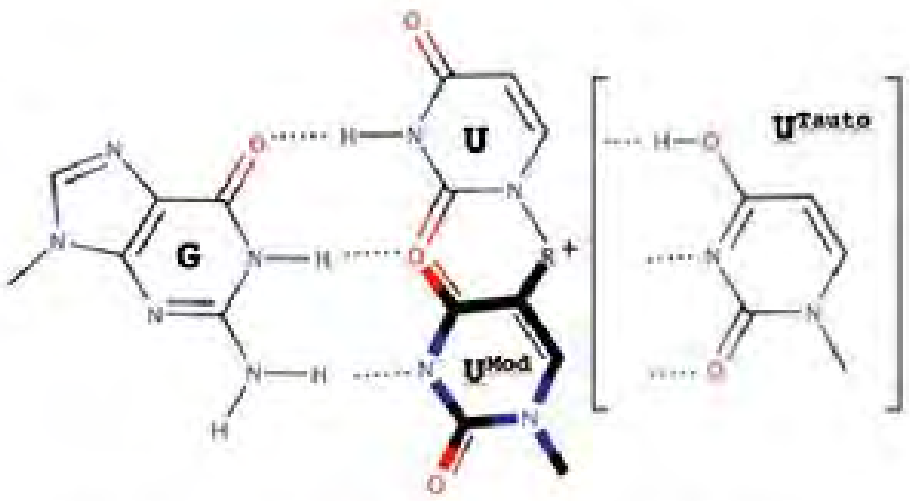
Three types of GoU pairs



The three observed types of GoU pairs in the ribosomal decoding center: the standard wobble (above), the Watson-Crick-like (left and right), and the minor groove GoU pair with U34 modified on C5 (noted U34 *).