GACcodonGGC: a very favorable context for translation errors?

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A survey of the literature on the effect of codon context on translation fidelity suggests that contexts such as GACcodonGGC are strong, but not unique, promotors of several types of translation errors.

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Our knowledge on the effect of codon context on the accuracy of translation is too uneven to make sweeping generalizations about the characteristics of a codon context which favors mistranslation. Nevertheless, we have observed highly suggestive 'coincidences', all in *Escherichia coli*. They are the following: (i) The extremely error-prone tryptophan codon of ribosomal protein S6 (0.004 cysteine per codon) is followed by GGC and preceded by GAC [1,2]. (ii) The extremely error-prone asparagine codon at position 12 of the RNA bacteriophage MS2 coat protein (0.004 lysine per codon) is followed by GGC and preceded by GAC. Conversely, none of the 3 accurately translated asparagine codons is preceded by GAC, GAU, GUA, GUG, or followed by GGC [3,4]. (iii) The extremely error-prone arginine codon of ribosomal protein L7/L12 (0.0015 cysteine per codon) is followed by GGC and preceded by GUA [1,5]. (iv) Out of 9 UGA codons whose efficiency of suppression had been studied by Miller and Albertini [6], 3 were very efficiently suppressed (i.e. about 8-times more frequently than the average for the 6 other UGAs). This high level of suppression was observed in both the absence and presence of the sup9 UGA suppressor. Two of these highly suppressed UGA codons (the most highly suppressed and the third most highly suppressed) were preceded by GAC. Conversely, none of the 6 inefficiently suppressed UGA codons were preceded by GAC, GAU, GUA or GUG, or followed by GG. (v) The mRNA for ribosomal protein L20, which we found to be very error-prone (0.02 cysteine per protein [7]) had 2 CGU codons preceded by a GAC [8] while proteins L1, L3, L13, L18, L33, S5, S7, S10 and S16, which were less error-prone [7], had no GAU codon and only one GAC codon in front of their 84 arginine codons [5,9–14].

The probability that the context GACcodonGGC be picked once or more in 2 random trials is 0.0023 (1 chance in 430), assuming that the frequency of occurrence of GAC and GGC codons in a gene is 36 per 1000 and 32 per 1000, respectively [15]. Considering together the highly error-prone codons of the ribosomal proteins S6, L7/L12, the MS2 coat protein and the 3 efficiently suppressed UGAs studied by Miller and Albertini [6], the probability of finding more than 2 GACs in front of 5 randomly chosen codons is 1 chance in 2300. We conclude that we are in the presence of a coincidence which is too striking to be immediately overlooked. It will be interesting to study, using site-directed mutagenesis techniques, the effect of the codon GAC, GGC and GUA on the accuracy of translation at tryptophan, arginine and other codons in other proteins. (It should be kept in mind, however, that the suppression of

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UAG codons was not preferentially stimulated by the presence of a 5′-GAC [16], suggesting that one should not expect all types of misincorporations to be indiscriminately stimulated by the presence of a GAC codon and its cognate tRNA 5′ to the A-site of the ribosome.)

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