A POSSIBLE EXPLANATION FOR INOSINE IN ANTICODONS

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In attempting to explain the near equivalence of 6-keto and 6-amino functions in RNA Traub and Elson (1966) have suggested that A - G pairs may occur in RNA. They emphasize that such A - G pairs, while sterically possible, would probably interrupt double-helix formation (i.e., standard base pairing) beyond the point of their occurrence owing to short contacts between the C_2 and N_3 atoms of the A and the C_2' sugar atom of the nucleotide in the 5' direction (see Fig. 1). If A - G pairs of this type do occur in RNA without appreciable distortion of the glycosidic bond distance between the two RNA chains, this type of bonding may also be feasible between tRNA and messenger RNA. Since base

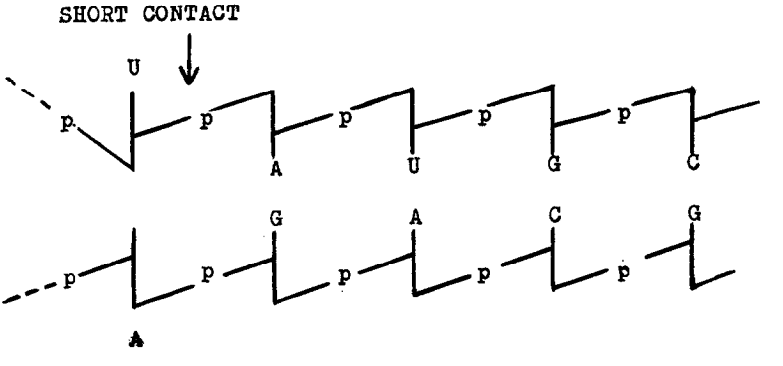

FIG. 1

pairing between tRNA and messenger RNA probably does not continue beyond the anticodon-codon contact, an A - G pair of the type shown in figure 2 would not interrupt codon-anticodon recognition and might be permitted in one order, but not the other. In like manner, A - G base pairs between $5'A_{codon}$ and $3'G_{anticodon}$ might be permitted between tRNA and messenger RNA. However A - G pairs between the middle bases of codons and anticodons would not be permitted since in either order these would distort codon-anticodon interaction.

The available evidence on the genetic code shows (Söll, Cherayil, and Bock, 1967) that recognition between the 5' position of codons and the 3' position of anticodons is extremely specific and does not permit "wobble" (Crick, 1966). This high degree of specificity may also exclude $5'A_{codon}$-$3'G_{anticodon}$ pairing between tRNA and messenger RNA. Thus the most likely site for A - G pairs between tRNA and messenger RNA is between $5'A_{anticodon}$ and $3'G_{codon}$. That is, the position at which "wobble" pairing is known to occur.

Examination of present coding assignments reveals that if 5'A in the anticodon could pair with 3'U or 3'G in messenger RNA considerable miscoding would result. For example, the normal tRNA for histidine (anticodon 5'AUG) would recognize codons for both histidine and glutamine (i.e., 5'CAU and 5'CAG). Such a situation would obviously be undesirable. Thus if A - G pairs <u>are</u> possible in tRNA-codon interaction, it would appear that these do not now occur and that A has been eliminated from the 5' position of anticodons in order to prevent miscoding. This might explain a) the existence of inosine in the 5' position of anticodons, resulting from the necessity to deaminate 5'A to prevent miscoding, and b) the failure to find the 3'U specific tRNA's predicted by the wobble hypothesis (Crick, 1966). $3'U_{codon}$ specific tRNAs

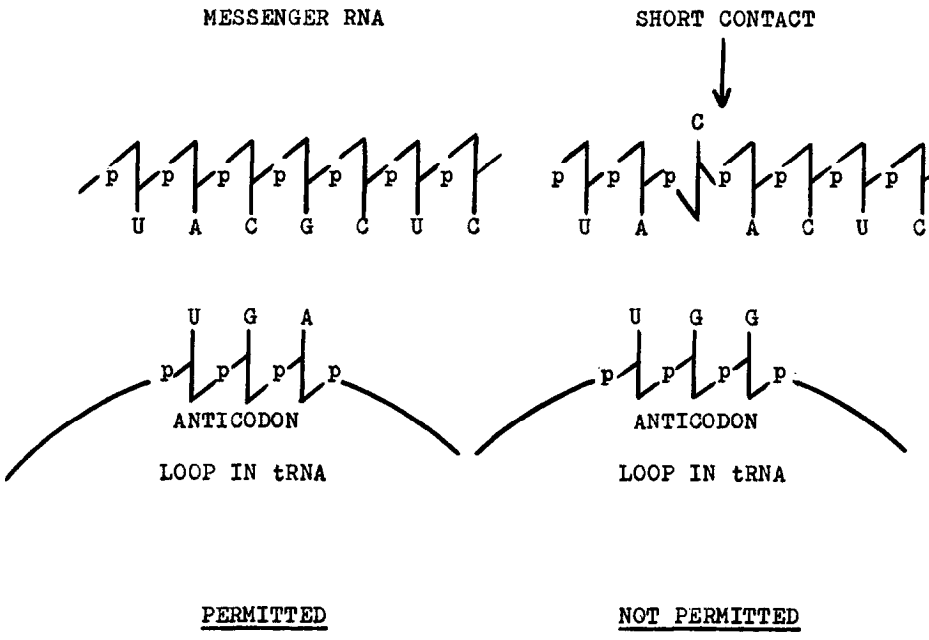

FIG. 2

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would contain $5'A_{anticodon}$ Because this would have permitted miscoding by $5'A_{anticodon}$-$3'G_{codon}$ pairing U specific tRNAs with anticodons carrying 5'A may have been eliminated.

If the above explanation is correct, it will be interesting to determine whether E. coli, which contains very little inosine in its tRNA, has resolved this problem by eliminating 5'A from the anticodons of its tRNA.

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