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Biological Role of Transfer Ribonucleic Acid Molecules

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The different known reactions in which transfer RNA is involved and the different enzymic alterations that may take place on this macromolecule will be summarized. Some aspects of the secondary and tertiary structure of transfer RNA and their relationship to transfer RNA function will also be examined. Finally, evidence for the induction of transfer RNA synthesis after T₄ bacteriophage infection will be presented.

The Effect on Transfer Ribonucleic Acid of Modification *in vitro*

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There have been many studies on the chemical modification of t-RNA* bases, and the resulting changes in the biological activity of these t-RNA species has been correlated with alterations in configuration or base sequence at specific sites in the molecule (Miura, 1967).

In this context, modification of t-RNA by chemical or enzymic overmethylation is of particular interest, since it has been shown that, in tumour tissue, t-RNA has an abnormal methylated base content (Borek, 1969).

By using conditions under which methylguanine is formed predominantly, *Escherichia coli* B t-RNA has been treated with dimethyl sulphate. Increasing levels of overmethylation, up to 13 moles % nucleotide excess, were used to study the physical behaviour of the t-RNA: in particular, the effects of over-methylation on melting curves and on optical rotatory dispersion have been examined.

Amino acid acceptance by overmethylated t-RNA was decreased by an amount characteristic for each of 18 of the common amino acids.

* Abbreviation: t-RNA, transfer RNA.

The formation of cysteinyl-t-RNA is an exception, which will be discussed. No evidence of mis-recognition at the amino acid acceptance level by overmethylated purified phenylalanyl-t-RNA was found.

The ability of purified phenylalanyl-t-RNA to bind to ribosomes (Nirenberg & Leder, 1964) was unimpaired by levels of methylation that inhibited its accepting ability by 55%. The formation *in vitro* of polyphenylalanine, polylysine and polypyrroline was considerably more sensitive to over-methylation of t-RNA than the corresponding amino acid-acceptance function. This suggests that the presence of additional methyl groups interferes with an activity of t-RNA other than amino acid acceptance or ribosome binding.

The use of a modifying method with considerable specificity for a particular base allows an attempt at interpretation of the biological effects of modification in terms of the involvement of defined areas in t-RNA. On this basis, some correlation has been attempted between modification of the anticodon and inhibition of amino acid acceptance: Weil, Befort, Rether & Ebel (1964) found no such correlation in yeast t-RNA. There is considerable evidence for and against the involvement of the anticodon region in aminoacyl-t-RNA synthetase recognition (e.g. Miura, 1967; Carbon & Curry, 1968) but recent work shows that such involvement is not a universal feature of the recognition system (Thiebe & Zachau, 1968; Geffer & Russell, 1969). This aspect will be fully discussed.

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