CHEMISTRY OF AMINOACYLATION OF 5'-AMP AND THE ORIGIN OF PROTEIN SYNTHESIS

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For many years our work centered around understanding the molecular basis for the origin of the genetic code. As that work progressed, it became more and more obvious that in order to understand the origin of coding, we needed to understand the origin of the process of protein synthesis. So, our work in the last few years has shifted to the study of chemical reactions and interactions related to the process of protein synthesis.

In contemporary protein synthesis, each amino acid is first activated by ATP and becomes an aminoacyl adenylate anhydride. From that compound, it is passed to become a 2' (3') ester of the 3' terminal 5'-AMP residue of tRNA. A new peptide bond is then formed between that amino acid ester and the growing peptide on an adjacent tRNA.

The chemistry of protein synthesis is thus the chemistry of aminoacyl AMP. Consequently much of our recent work has been a study of aminoacyl AMP derivatives. Elucidation of the character of aminoacyl AMP reactions has made it obvious that AMP (and perhaps other purine monoribonucleotides) has characteristics which should allow it to preferentially catalyze the synthesis of L-amino acid peptides. The essential features which lead to this conclusion are: (1) all L-amino acids (but not all D amino acids) when esterified to 5'-AMP preferentially (65%) distribute to the 3' position of the 5'-AMP. (2) esterification is predominantly at the 2' position. (3) 2', 3' diaminoacyl esters are readily formed. (4) a peptide bond can be formed between adjacent 2', 3' aminoacyl esters.

The experimental data concerning these characteristics of 5'-AMP will be presented with discussion of how they may have served to direct the origin and evolution of protein synthesis, including the use of L-amino acids.