

# **Ala-His mediated peptide bond formation revisited.**

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The historical origin of the translation machinery remains unresolved. Although the large 23S ribosomal RNA (rRNA) is almost certainly the catalytic component of the peptidyl transferase center in the modern ribosome, it is likely that greatly simplified systems were initially employed in the late stages of the prebiotic world. In particular, it has been suggested that small RNAs carrying amino acids were important for the genesis of protein synthesis. Consistent with this, a dipeptide, Ala-His, was previously claimed to be a prebiotically feasible catalyst mediating peptide bond formation in the presence of aminoacylated tRNA and cognate mRNA template, in the absence of other ribosomal components (Shimizu, 1996). We herein report a detailed study of putative dipeptide formation by Ala-His and RNAs carrying leucine. Based on the results presented here, it is unlikely that the dipeptide, Ala-His, catalyzes significant levels of Leu-Leu dipeptide formation in solution. A product is produced which can be readily mistaken for a dipeptide in the TLC separation systems employed in earlier work. We offer explanations for the formation of this product as well as another unexpected product. The results presented here are consistent with the notion that the translation machinery was likely based on catalytic RNA from its very inception.

PMID: 11770259 [PubMed - indexed for MEDLINE]