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Norvaline and norleucine may have been more abundant protein components during early stages of cell evolution

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Introduction: The nature of the evolutionary process that led to the selection of the L α-amino acids found in proteins is an unsolved issue in the study of the origin of life. Major prebiotic products are absent from the inventory of protein amino acids. We discuss the case of two hydrophobic amino acids: norvaline and norleucine.

L-Norvaline and L-Norleucine are incorporated into proteins: The intracellular accumulation of norleucine and norvaline results from the low-substrate specificity of the branched-chain amino acid pathway enzymes [4, 5]. Under anaerobic conditions, such as those that likely existed in the primitive environment prior to the development of an oxidizing atmosphere, high glucose concentrations lead to a rapid accumulation of pyruvate, which is immediately used as an alternative substrate for direct keto chain elongation to α-ketobutyrate first, and then to α-ketovalerate which undergoes transamination and forms L-norvaline [6]. Norleucine is also a by-product of the leucine biosynthetic pathway enzymes starting from pyruvate or α-ketoisovalerate, and can be misincorporated in place of methionine in recombinant proteins [5].

Conclusions: The exhaustion of the prebiotic budget of norvaline, norleucine and other non-proteinic amino acids did not stop their misincorporation into proteins. The mechanisms described here may have operated during the early stages of biochemical evolution, but continued afterwards when the development of the biosynthesis of branches-chain amino acids led to norvaline and norleucine as by-products [7].

The incorporation in proteins of norvaline in place of leucine is an outcome of the combination of the substrate ambiguity and multifunctionality of both leucyl-tRNA synthase and the branched-chain amino acid biosynthetic enzymes. Such functional flexibilities may confer evolutionary advantages, especially under anaerobic conditions that favor the accumulation of pyruvate.

References:

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