Abstract:
Two vitamins, biotin and lipoic acid, are essential in all three domains of life. Both coenzymes function only when covalently attached to key metabolic enzymes. There they act as “swinging arms” that shuttle intermediates between two active sites (= covalent substrate channeling) of key metabolic enzymes. Although biotin was discovered over 100 years ago and lipoic acid 60 years ago, it was not known how either coenzyme is made until recently. In Escherichia coli the synthetic pathways for both coenzymes have now been worked out for the first time.

The late steps of biotin synthesis, those involved in assembling the fused rings, were well-described biochemically years ago. In contrast, the early steps of biotin synthesis, assembly of the fatty acid-like “arm” of biotin were unknown. It has now been demonstrated that the arm is made by using disguised substrates to gain entry into the fatty acid synthesis pathway followed by removal of the disguise when the proper chain length is attained. The BioC methyltransferase is responsible for introducing the disguise and the BioH esterase for its removal.

In contrast to biotin, which is attached to its cognate proteins as a finished molecule, lipoic acid is assembled on its cognate proteins. An octanoyl moiety is transferred from the octanoyl-ACP of fatty acid synthesis to a specific lysine residue of a cognate protein by the LipB octanoyl transferase followed by sulfur insertion at carbons C6 and C8 by the LipA lipoyl synthetase.