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Progress in Lipid Research 44 (2005) 125–153
Progress in Lipid Research
www.elsevier.com/locate/plipres

Review

Coenzyme A: Back in action

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Abstract

Coenzyme A (CoA) is a ubiquitous essential cofactor that plays a central role in the metabolism of carboxylic acids, including short- and long-chain fatty acids. In the last few years, all of the genes encoding the CoA biosynthetic enzymes have been identified and the structures of several proteins in the pathway have been determined. CoA is assembled in five steps from pantothenic acid and pathway intermediates are common to both prokaryotes and eukaryotes. In spite of the identical biochemistry, remarkable sequence differences among some of the prokaryotic and eukaryotic enzymes have been revealed by comparative genomics. Renewed interest in CoA has arisen from the realization that the biosynthetic pathway is a target for antibacterial drug discovery and from the unexpected association of a human neurodegenerative disorder with mutations in pantothenate kinase. The purpose of this review is to integrate previous knowledge with the most recent findings in the genetics, enzymology and regulation of CoA biosynthesis in bacteria, plants and mammals.

Keywords: Coenzyme A; Pantothenic acid; Vitamin; Pantothenate kinase; Intermediary metabolism; Cofactor

Contents

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doi:10.1016/j.plipres.2005.04.001

1. Introduction

1.1. The biochemical pathway for coenzyme A biosynthesis

Coenzyme A (CoA) is an indispensable cofactor in all living organisms, where it functions as an acyl group carrier and carbonyl-activating group in a number of central biochemical transformations, including the tricarboxylic acid cycle and fatty acid metabolism. About 4% of known enzymes utilize CoA as an obligate cofactor and CoA is involved in over 100 different reactions in intermediary metabolism [1,2]. CoA is the source of 4′-phosphopantetheine, the prosthetic group of carrier proteins of fatty acid, polyketide and nonribosomal peptide synthases [3–5]. The biosynthesis of CoA from pantothenic acid is an essential and universal pathway in prokaryotes and eukaryotes. The CoA biosynthetic genes in bacteria, plants and mammals are known; however, there are some exceptions that will be highlighted in the review. CoA is assembled in five steps