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Alanine and inter-organ relationships in branched-chain amino and 2-oxo acid metabolism. Review.

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Abstract

Branched-chain amino acid metabolism in skeletal muscle promotes the production of alanine, an important precursor in hepatic gluconeogenesis. There is controversy concerning the origin of the carbon skeleton of alanine produced in muscle, specifically whether it is derived from carbohydrate via glycolysis (the glucose-alanine cycle) or from amino acid precursors (viz. glutamate, valine, isoleucine, methionine, aspartate, asparagine) via a pathway involving phosphoenolpyruvate (PEP) carboxykinase and pyruvate kinase, or NADP-malate dehydrogenase (malic enzyme). The relevant literature is reviewed and it is concluded that neogenic flux from amino acids is unlikely to be of major quantitative importance for provision of the carbon skeleton of alanine either in vitro or in vivo. Evidence is presented that branched-chain amino acid oxidation in muscle is incomplete and that the branched-chain 2-oxo acids and the products of their partial oxidation (including glutamine) are released. The role of these metabolites is discussed in the context of fuel homeostasis in starvation.

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