

## Review

# Primary Roles of Branched Chain Amino Acids (BCAAs) and Their Metabolism in Physiology and Metabolic Disorders

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**Abstract:** Leucine, isoleucine, and valine are collectively known as branched chain amino acids (BCAAs) and are often discussed in the same physiological and pathological situations. The two consecutive initial reactions of BCAA catabolism are catalyzed by the common enzymes referred to as branched chain aminotransferase (BCAT) and branched chain  $\alpha$ -keto acid dehydrogenase (BCKDH). BCAT transfers the amino group of BCAAs to 2-ketoglutarate, which results in corresponding branched chain 2-keto acids (BCKAs) and glutamate. BCKDH performs an oxidative decarboxylation of BCKAs, which produces their coenzyme A-conjugates and NADH. BCAT2 in skeletal muscle dominantly catalyzes the transamination of BCAAs. Low BCAT activity in the liver reduces the metabolization of BCAAs, but the abundant presence of BCKDH promotes the metabolism of muscle-derived BCKAs, which leads to the production of glucose and ketone bodies. While mutations in the genes responsible for BCAA catabolism are involved in rare inherited disorders, an aberrant regulation of their enzymatic activities is associated with major metabolic disorders such as diabetes, cardiovascular disease, and cancer. Therefore, an understanding of the regulatory process of metabolic enzymes, as well as the functions of the BCAAs and their metabolites, make a significant contribution to our health.

**Keywords:** branched chain aminotransferase; branched chain  $\alpha$ -keto acid dehydrogenase; ketogenesis; gluconeogenesis; diabetes; cancer



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## 1. Introduction

Amino acids are the sources of biological components such as proteins, nucleic acids, and bioactive amines in anabolic reactions, and they also are the primary energy substrates in catabolic reactions during both periods of fasting and sustained exercise. Among hundreds of amino acids, twenty are considered to be the building blocks of proteins, and these are metabolized according to corresponding nutritional requirements. In humans, almost half of the proteinaceous amino acids cannot be synthesized from metabolic intermediates and must be consumed in food [1,2]. Leucine (Leu), isoleucine (Ile), and valine (Val) are essential amino acids and are collectively referred to as branched chain amino acids (BCAAs) because they have branched structures in their side chains and uniquely share two of the initial metabolic pathways. Muscular proteins are dominantly built with BCAAs, which make up 20% to 25% of all amino acids in dietary proteins and play primary roles in muscular function [1,2].

The first process of BCAA catabolism catalyzed by branched chain aminotransferase (BCAT) and the second process catalyzed by branched chain  $\alpha$ -keto acid dehydrogenase

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