論　文　要　旨

（ Induction of PDK4 in the heart muscle of JVS mice, an animal model of systemic carnitine deficiency, does not appear to reduce glucose utilization by the heart ）

牛飼　美晴

Abstract

Pyruvate dehydrogenase kinase 4 (PDK4) mRNA has been reported as an up-regulated gene in the heart and skeletal muscle of carnitine-deficient juvenile visceral steatosis (JVS) mice under fed conditions. PDK4 plays an important role in the inhibition of glucose oxidation via the phosphorylation of pyruvate dehydrogenase complex (PDC). This study evaluated the meaning of increased PDK4 mRNA in glucose metabolism by investigating PDK4 protein levels, PDC activity and glucose uptake by the heart and skeletal muscle of JVS mice. PDK4 protein levels in the heart and skeletal muscle of fed JVS mice were increased in accordance with mRNA levels, and protein was enriched in the mitochondria. PDK4 protein was co-fractionated with PDC in sucrose density gradient centrifugation, like PDK2 protein; however, the activities of the pyruvate dehydrogenase complex (PDC) active form in the heart and skeletal muscle of fed JVS mice were similar to those in fed control mice. Fed JVS mice showed significantly higher glucose uptake in the heart and similar uptake in the skeletal muscle compared with fed control mice. Thus, in carnitine deficiency under fed conditions, glucose was preferentially utilized in the heart as an energy source despite increased PDK4 protein levels in the mitochondria. The preferred glucose utilization may be involved in developing cardiac hypertrophy from carnitine deficiency in fatty acid oxidation abnormality.