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A novel congenital muscular dystrophy with mitochondrial structural abnormalities caused by defective *de novo* phosphatidylcholine biosynthesis

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Background: A decade ago, we reported four patients from three families with a new "congenital muscular dystrophy with mitochondrial structural abnormalities (CMDmt)" whose muscle pathology was characterized by the enlargement of mitochondria at the periphery of but the depletion of mitochondria in the center of muscle fibers. All patients had severe mental retardation.
Objective: To identify causative gene for CMDmt.
Methods: We sequenced *CHKB* gene which encodes human choline kinase beta because rostrocaudal muscular dystrophy (*rmd*) mice due to a loss-of-function mutation *Chkb* gene that encodes choline kinase beta, the first step enzyme in phosphatidylcholine (PC) biosynthetic pathway, show a similar unique mitochondrial abnormality to that of CMDmt patients. We also measured choline kinase activity and PC level in patient muscles.
Results: We identified homozygous or compound heterozygous mutations in *CHKB* gene. Enzymatic activity was not detected and PC was significantly decreased in patient's muscles.
Conclusion: CMDmt is caused by loss-of-function mutations in *CHKB* gene. This is the first human disease caused by disruption of a phospholipid *de novo* biosynthetic pathway, demonstrating the pivotal role of phosphatidylcholine in muscle and brain.

生体膜の主要構成リン脂質ホスファチジルコリンを合成するコリンキナーゼの機能喪失遺伝子変異により、ヒトの筋ジストロフィーが引き起こされることが判明した。