A novel regulator of carnitine transporter: its structure and function

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It is reported that in patients with chronic fatigue syndrome (CFS), serum levels of acetylcarnitine are decreased, and that administration of acetylcarnitine improves symptoms of these patients (Kuratsune et al., unpublished data). Moreover, the study using positron emission tomography (PET) has shown that acetylcarnitine is specifically transported into the human brain, and that the specific uptake is low in patients with CFS (1). These data strongly suggest that a decrease in acetylcarnitine transport into neuronal or glial cells of the brain plays an important role in the pathogenesis of CFS. Recently cDNA encoding carnitine transporter (OCTN2) has been cloned from cDNA libray of the human kidney (2). This molecule is present on the cell membrane and transports acetylcarnitine into the cell in addition to carnitine. The expression of the transporter is high in the tissues such as kidney, skeletal muscle, heart, placenta and pancreas, but it is low or null in the brain. Thus mutations in the gene for OCTN2 cause systemic manifestations (called primary systemic carnitine deficiency, SCD) such as cardiomyopathy, skeletal myopathy, hypoketotic hypoglycemia and hyperammonaemia (3, 4). In thepresent study, we attempted to isolate the cDNA for brain-specific acetylcarnitine transporter. For this purpose, we screened a rat brain cDNA library (2.0×10^6 pfu) using a part of cDNA for OCTN2 as a probe. Fifteen positive clones were obtained and their sequences were determined: nine and four clones encoded OCTN2 and OCTN1, respectively, whereas the remaining two were found to encode novel molecules (designated OCTNRα and β). These molecules by themselves had no transporting activity for carnitine and acetylcarnitine, but they had the ability to strongly modulate the transporting activity of OCTN2. In the conference, we will describe the molecular structure, function, tissue distribution and functional significance.

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2) Tamai I, et al. (1998) J Biol Chem 273, 20378-20382.
3) Nezu J, et al. (1999) Nature Genet 21, 91-94.
4) Wang Y, et al. (1999) Proc Natl Acad Sci USA 96, 2356-2360.