Genomic and nongenomic regulation of mitochondrial fat oxidation

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The regulation of mitochondrial fat import and oxidation is under both genomic and nongenomic control. Using the rainbow trout model, we examined transcriptional regulation and the effects of membrane composition and fluidity on the regulation of carnitine palmitoyltrasferase (CPT) I by its allosteric inhibitor malonyl-CoA. Sensitivity of CPTI to regulation (IC_{50}) was found to correlate with membrane properties of fluidity (PC:PE, %DHA) but trout enzyme kinetics were opposite to that in mammals, with liver CPTI more sensitive to malonyl-CoA than muscle. Interestingly, when measured directly, membrane fluidity was unchanged with fasting but IC_{50} increased both in muscle and liver. Tissue- and species-specific differences in CPTI kinetics may be linked to an increased diversity in CPTI isoforms expressed in trout due to repeated genome duplication events in fish lineages. In trout five isoforms are expressed in all tissue examined and these isoforms show nucleotide and amino acid substitutions potentially important for diversity in malonyl-CoA binding and interaction with membrane lipids.