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EFFECTS OF A CHOLINE DEFICIENT DIET ON ENERGY EXPENDITURE IN MICE

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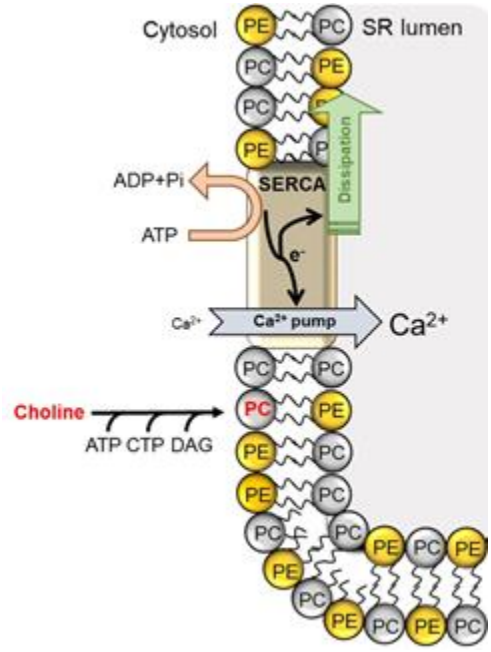
Background



The energy efficiency of skeletal muscle has been shown to be an important part of regulating weight in both humans and in mice (3). Myosin-ATPase, Na^{2+}/K^{+}-ATPase, and sarco/endoplasmic reticulum Ca^{2+} -ATPase (SERCA) are the three classes of ATPase that account for most of the energy expenditure by skeletal muscle. Ca^{2+} ions are transported across the gradient between cytosol and the sarco/endoplasmic reticulum lumen. The activity of SERCA ATPase is about 40-50% of muscle resting metabolic rate and 15-20% of the energy expenditure of the whole body (2). This means something that could affect the SERCA efficiency of muscles might have a big effect on the entire body's metabolic rate. The normal stoichiometry for pumping Ca^{2+} ions is two ions to every one molecule of ATP that is hydrolyzed. This process could be reduced to make SERCA pump less efficiently which would require the body to work harder, increasing the overall energy expenditure. Membrane lipid composition, Ca^{2+} concentration, and SERCA-interacting peptides are a few factors that affect SERCA function in the muscles (6). Sarcolipin, which interacts with SERCA, regulates SERCA energy efficiency and it has been found that when it is absent from skeletal muscle in mice there is an increased metabolic rate and the mice don't suffer from diet-induced obesity (7).

Phospholipid composition of SERCA also affects energy efficiency of SERCA. Phosphatidylethanolamine (PE) and phosphatidylcholine (PC) are two lipids in muscle sarcoplasmic reticulum that affect SERCA activity. PE methyltransferase (PEMT) acts as a catalyst in a reaction that forms PC from PE (4). Mice that can't perform PE methylation (PEMTKO mice), have an increased energy expenditure which protects the mice from diet-induced obesity. Our laboratory has found that skeletal muscles from PEMTKO mice have a decreased SERCA transport efficiency and an increased O_2 consumption. These observations were recapitulated in mice with tamoxifen-inducible skeletal muscle specific knockout of PEMT (PEMT-MKO). Thus, phospholipid composition of muscle SR appears to affect energy expenditure and propensity for diet-induced obesity.

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