Steatosis and Mitochondria: Impact of Lipid Oxidation on Bioenergetics and Reactive Oxygen Species Production

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Steatosis involves triacylglycerol accumulation in hepatocytes and is a common disease that is associated with metabolic malfunctions and obesity. The main pathways that oxidize lipids in the liver are mitochondrial, and mitochondria are known to play a central role in steatosis. Here we studied the mitochondrial effects of short-term high-fat diets in mice and found that liver mitochondria isolated from mice on high-fat diets produce significantly more H$_2$O$_2$ (measured by the Amplex Red method) when respiring on palmitoyl-CoA, but not octanoyl-CoA nor butyryl-CoA. Palmitoyl-carnitine also promoted enhanced respiratory rates in mitochondria from animals on a high fat diet. Those changes were reversed by malonyl-CoA, which inhibits the transport of palmitoyl-CoA into the mitochondrial matrix. Western blot analysis determined that acyl-CoA dehydrogenases were increased in mice on this diet. Altogether, these results indicate that acyl-CoA dehydrogenases may be overexpressed as an adaptive response to lipid insult in steatosis and that very long chain acyl-CoA dehydrogenase is a novel, diet-sensitive, and significant source of ROS in mitochondria.

Keywords: Mitochondria, Reactive Oxygen Species, Acyl-CoA dehydrogenases
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