Acylcarnitines: Linking Fatty Acid-Derived Energy Metabolites to Diet, Lifestyle, and Redox Balance

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Acylcarnitines, the esters of carnitine and fatty acids, are key intermediates of fatty acid metabolism. While the fundamental role of carnitine in mitochondrial long-chain fatty acid transport is well established, the physiological functions of specific acylcarnitines and the significance of their chain-length diversity remain only partly understood.

L-carnitine, discovered more than a century ago by Latvian biochemist R. Krimberg, is both an essential biofactor for mitochondrial β-oxidation and a widely used nutritional supplement, valued for its safety and potential effects on energy metabolism. However, efficient stimulation of fatty acid oxidation requires high intracellular concentrations, whereas carnitine bioavailability under normal physiological conditions is relatively limited. Supplementation with high doses of L-carnitine alters systemic metabolite levels, particularly trimethylamine-N-oxide and acylcarnitines.

Advances in mass spectrometry now allow comprehensive profiling of carnitine and acylcarnitines, opening new perspectives on their roles in health and disease. Acylcarnitine analysis is already applied in clinical practice, most notably in newborn screening for inborn errors of fatty acid oxidation. Accumulation of specific long-chain or very-long-chain acylcarnitines serves as a biomarker of defective β-oxidation enzymes, including mitochondrial trifunctional protein.

Physiologically, plasma acylcarnitine concentrations fluctuate with fasting–feeding cycles and the availability of fatty acids and glucose. Elevated long-chain acylcarnitine levels have been shown to impair insulin signaling and mitochondrial function, promoting excessive reactive oxygen species production—effects that are reversible when concentrations decline. Nutritional status and lifestyle factors, including physical activity, also modulate acylcarnitine profiles, emphasizing their dynamic link to metabolism and redox regulation.

Growing evidence highlights the importance of defining physiological versus pathological thresholds for acylcarnitines. A deeper understanding of their diverse roles in cellular processes may provide novel biomarkers and therapeutic opportunities, bridging the exposome, redox biology, and metabolic health.