Abstract

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Short Chain Fatty Acid Acetate Increases TNFα-Induced MCP-1 Production in Monocytic Cells via ACSL1/MAPK/NF-κB Axis

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Abstract

Short-chain fatty acid (SCFA) acetate, a byproduct of dietary fiber metabolism by gut bacteria, has multiple immunomodulatory functions. The anti-inflammatory role of acetate is well documented; however, its effect on monocyte chemoattractant protein-1 (MCP-1) production is unknown. Similarly, the comparative effect of SCFA on MCP-1 expression in monocytes and macrophages remains unclear. We investigated whether acetate modulates TNFα-mediated MCP-1/CCL2 production in monocytes/macrophages and, if so, by which mechanism(s). Monocytic cells were exposed to acetate with/without TNFα for 24 h, and MCP-1 expression was measured. Monocytes treated with acetate in combination with TNFα resulted in significantly greater MCP-1 production compared to TNFα treatment alone, indicating a synergistic effect. On the contrary, treatment with acetate in combination with TNFα suppressed MCP-1 production in macrophages. The synergistic upregulation of MCP-1 was mediated through the activation of long-chain fatty acyl-CoA synthetase 1 (ACSL1). However, the inhibition of other bioactive lipid enzymes [carnitine palmitoyltransferase I (CPT I) or serine palmitoyltransferase (SPT)] did not affect this synergy. Moreover, MCP-1 expression was significantly reduced by the inhibition of p38 MAPK, ERK1/2, and NF-κB signaling. The inhibition of ACSL1 attenuated the acetate/TNFα-mediated phosphorylation of p38 MAPK, ERK1/2, and NF-κB. Increased NF-κB/AP-1 activity, resulting from acetate/TNFα co-stimulation, was decreased by ACSL1 inhibition. In conclusion, this study demonstrates the proinflammatory effects of acetate on TNF-α-mediated MCP-1 production via the ACSL1/MAPK/NF-κB axis in monocytic cells, while a paradoxical effect was observed in THP-1-derived macrophages.

Biography

A chemical engineer with an MSc in advanced chemical engineering form the University of Birmingham, UK. Currently working with the immunology and microbiology lab at Dasman Diabetes Insitute with a focus on identifying novel metabolic makers and signaling pathways associated with the type 2 diabites and its related complications. He was Senior Research Associate of Council of Scientific and Industrial Research (CSIR), Government of India. He qualified National Eligibility Test (NET) of Government of India & received full fellowship for Doctoral research.

