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ATP Release Drives Inflammation with Lysophosphatidylcholine

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Free article

Abstract

Lysophosphatidylcholine (LPC), a dominant lipid component of oxidized low-density lipoprotein, plays a major role in inflammation associated with atherosclerosis and neurodegenerative disorders. It activates inflammatory responses from macrophages, neuronal cells, and endothelial cells. However, the exact mechanism by which LPC promotes inflammation remains incompletely understood. In this study, we show that the production of inflammatory cytokines and cytotoxicity with LPC are both critically dependent on its ability to bring about release of ATP from cells. The induction of caspase-1-mediated IL-1β release with LPC from TLR-primed mouse and human macrophages and mouse neuronal cells is reduced in the presence of ATP-hydrolyzing enzyme, apyrase, and the inhibitors of purinergic signaling. ATP released from LPC-treated cells also promotes an IL-12p70^{hi}, low phagocytic, and poorly costimulatory phenotype in macrophages in a caspase-1-independent manner. Treatment with

apyrase reduces production of inflammatory cytokines with LPC in vivo. These findings reveal a previously unappreciated pathway for the generation of inflammatory responses with LPC, and these have significant implications for therapeutic intervention in chronic inflammatory disorders promoted by this lipid.