JOURNAL OF LEUKOCYTE BIOLOGY

Spotlight on Leading Edge Research

Frontline Science: Tumor necrosis factor - α stimulation and priming of human neutrophil granule exocytosis

Kenneth R. McLeish, Michael L. Merchant, ... See all authors ›

First published: 17 January 2017
https://doi.org/10.1189/jlb.3HI0716-293RR
Cited by:5

Abstract

Neutrophil granule exocytosis plays an important role in innate and adaptive immune responses. The present study examined TNF - α stimulation or priming of exocytosis of the 4 neutrophil granule subsets. TNF - α stimulated exocytosis of secretory vesicles and gelatinase granules and primed specific and azurophilic granule exocytosis to fMLF stimulation. Both stimulation and priming of exocytosis by TNF - α were dependent on p38 MAPK activity. Bioinformatic analysis of 1115 neutrophil proteins identified by mass spectrometry as being phosphorylated by TNF - α exposure found that actin cytoskeleton regulation was a major biologic function. A role for p38 MAPK regulation of the actin cytoskeleton was confirmed experimentally. Thirteen phosphoproteins regulated secretory vesicle quantity, formation, or release, 4 of which—Raf1, myristoylated alanine - rich protein kinase C (PKC) substrate (MARCKS), Abelson murine leukemia interactor 1 (ABI1), and myosin VI—were targets of the p38 MAPK pathway. Pharmacologic inhibition of Raf1 reduced stimulated exocytosis of gelatinase granules and priming of specific granule exocytosis. We conclude that differential regulation of exocytosis by TNF - α involves the actin cytoskeleton and is a necessary component for priming of the 2 major neutrophil antimicrobial defense mechanisms: oxygen radical generation and release of toxic granule contents.

Citing Literature

Supporting Information