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Ceramide Induces the Generation of Reactive Oxygen Species in Activated RAW 264.7 Murine Macrophage Cells

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Ceramide acts as a lipid second messenger in the cellular signal transduction and is involved in mediating a variety of cellular functions such as differentiation, growth regulation and apoptosis. In the present study, we have investigated the effect of ceramide on the generation of reactive oxygen species (ROS) in RAW 264.7 murine macrophage cells to understand the relationship between ceramide-mediated cell cytotoxicity and ROS production. Treatment with C₆-ceramide or bacterial sphingomyelinase significantly enhanced the production of ROS in RAW 264.7 cells activated with bacterial lipopolysaccharide (LPS) and interferon-gamma. The generation of ROS was increased in a dose-dependent manner with ceramide treatment to LPS and interferon-gamma-treated cells. Intracellular glutathione level was suppressed by ceramide in activated cells. The elevated level of ROS was significantly decreased in the presence of diphenyleneiodonium chloride, a NADPH oxidase inhibitor. From the proteomic analyses, we found that ceramide increased the expression of vimentin, T-cell receptor α -chain, α , and β -actin in LPS and interferon-gamma-activated RAW 264.7 cells. Taken together, these studies suggest that ceramide-mediated enhanced ROS generation may regulate the cellular signaling and induce changes in various protein synthesis in LPS and interferon-gamma-activated RAW 264.7 cells.

Keyword : ceramide, reactive oxygen species, RAW