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Ceramide 1-phosphate is a novel regulator of cell migration: Implication in inflammatory responses

Ceramide 1-phosphate (C1P) is a bioactive sphingolipid with mitogenic, prosurvival, and proinflammatory properties. More recently, we showed that C1P promotes cell migration. However, the mechanisms involved in these actions are only beginning to be elucidated. Using murine and human macrophages we have now discovered a new biological activity of C1P: stimulation of monocyte chemoattractant protein-1 (MCP-1) release. This novel effect of C1P is pertussis toxin (Ptx)-sensitive, suggesting the intervention of Gi protein-coupled receptors in this action. Treatment of the macrophages with C1P caused activation of the phosphatidylinositol 3-kinase (PI3K)/protein kinase B (PKB, also known as Akt), mitogen-activated protein kinase kinase (MEK)/extracellularly regulated kinases (ERK), and p38 pathways. Of interest, inhibition of these kinases with specific siRNAs to silence the genes encoding these enzymes, or with selective pharmacological inhibitors blocked the stimulation of MCP-1 release. In addition, we found that C1P stimulated nuclear factor-kappa B activity, and that blockade of this transcription factor also resulted in complete inhibition of MCP-1 release. Noteworthy, C1P stimulated MCP-1 release and cell migration in adipocytes. A key observation was that sequestration of MCP-1 with a neutralizing antibody, or treatment with MCP-1 siRNA abolished C1P-stimulated cell migration. A second key observation was that inhibition of the signaling pathways involved in C1P-stimulated MCP-1 release completely blocked the stimulation of cell migration by C1P. It can be concluded that C1P promotes MCP-1 release in different cell types and that this chemokine is a major mediator of C1P-stimulated cell migration.

Biography

Antonio Gomez-Munoz completed his Ph.D. at the University of the Basque Country (Bilbao, Spain) in 1988. He then started postdoctoral training at the University of Alberta, in Edmonton (Alberta), and continued his training at the University of British Columbia in Vancouver (British Columbia), both in Canada. He has published more than 70 papers in reputed journals and various book chapters. At present, he is a Professor of Biochemistry and Molecular Biology at the University of the Basque Country in Bilbao (Spain).

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