

12/15-リポキシゲナーゼで合成される脂質シグナル分子の病態生理機能

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Pathophysiological role of lipid molecules produced by 12/15-lipoxygenase

Research Project

Project/Area Number

12470024

Research Category

Grant-in-Aid for Scientific Research (B)

Allocation Type

Single-year Grants

Section

一般

Research Field

General medical chemistry

Research Institution

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Lipoxygenase / Macrophage / Oxidized LDL / LDL receptor-related protein / Cholesterol ester / Translocation

Research Abstract


Lipoxygenase incorporates a molecular oxygen regioselectively and stereoselectively into unsaturated fatty acids. There are four classes of enzymes in mammalian tissues; 5-, 8-, 12-, and 15-lipoxygenases, named by the number indicating oxygenation site of arachidonic acid as a substrate. Among the enzymes, 12-lipoxygenases are widely distributed in various tissues and species, and there are three isoforms: platelet, leukocyte and epidermis types. Since the leukocyte 12-lipoxygenase and 15-lipoxygenase-1 are highly related in their primary structures and enzymological properties, these enzymes are collectively called as 12/15-lipoxygenase. A number of evidences support the role of 12/15-lipoxygenase in LDL oxidation. In order to investigate precise mechanisms of the 12/15-lipoxygenase-mediated LDL oxidation, we established a mouse macrophage-like J774A1 cell line overexpressing porcine leukocyte 12-lipoxygenase. The presence of regio- and stereoselectively oxygenated product of cholesteryl linoleate in the LDL indicates that the 12/15-lipoxygenase is responsible for cell-mediated LDL oxidation. We also showed that LDL receptor-related protein


(LRP) was required for the enzyme-mediated LDL oxidation by macrophages. Furthermore, cholesterol ester selectively transferred from the LDL particle to the plasma membrane via LRP is oxygenated by 12/15-lipoxygenase translocated to this membrane:


Research Products (13 results)


All Other

All Publications


[Publications] Kawajiri H, Zhuang D-M, Qiao N, Yoshimoto T, Yamamoto M, et al.: "Expression of arachidonate 12-lipoxygenase in rat tissues : Role of the enzyme in glucagon secretion" *J Histochem Cytochem.* 48. 1411-1420 (2000) 


[Publications] Zhuang D-M, Kawajiri H, Takahashi Y, Yoshimoto T: "Suppression of prostaglandin E2-mediated c-fos mRNA induction by interleukin-4 in murine macrophages" *J Biochem.* 127. 451-456 (2000) 


[Publications] Xu W, Takahashi Y, Sakashita T, Iwasaki T, Hattori H, et al.: "Low density lipoprotein receptor-related protein is required for macrophage-mediated oxidation of low density lipoprotein by 12/15-lipoxygenase" *J Biol Chem.* 276. 36454-36459 (2001) 


[Publications] Kadoyama K, Takahashi Y, Higashida H, Tanabe T, et al.: "Cyclooxygenase-2 stimulates production of amyloid β -peptide in neuroblastoma x glioma hybrid NG108-15 cells" *Biochem Biophys Res Commun.* 281. 483-490 (2001) 


[Publications] Yoshimoto T, Takahashi Y: "Arachidonate 12-lipoxygenases" *J Lipid Med and Cell Signal.* 168-69. 245-262 (2002) 


[Publications] Zhu H, Takahashi Y, Xu W, Kawajiri H, Murakami T, et al.: "Low density lipoprotein receptor-related protein-mediated membrane translocation of 12/15-lipoxygenase is required of oxidation of low density lipoprotein by macrophages" *J Biol Chem.* 278. 13350-13355 (2003) 

[Publications] 吉本谷博: "基礎生化学実験法(分担執筆)" *東京化学同人(日本生化学会編).* 338 (2000) 


[Publications] Kawajiri H., Zhuang D.-M., Qiao N., Yoshimoto T., Yamamoto M., Iseki S. and Hamaguchi K.: "Expression of arachidonate 12-lipoxygenase in rat tissues: Role of the enzyme in glucagon secretion" *J Histochem Cytochem.* 48. 1411-1420 (2000) 

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[Publications] Xu W., Takahashi Y., Sakashita T., Iwasaki T., Hattori H. and Yoshimoto T.: "Low density lipoprotein receptor-related protein is required for macrophage-mediated oxidation of low density lipoprotein by 12/15-lipoxygenase" *J Biol Chem.* 276. 36454-36459 (2001) 

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