

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

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2002 Fiscal Year Final Research Report Summary

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

Kanazawa University

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Keywords

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

Research Abstract

Lipoxygenase incorporates a molecular oxygen regiospecifically and stereospecifically 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 stereospecifically 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)

AllOther

AllPublications

[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] Yoshimoto T. and Takahashi Y.: "Arachidonate 12-lipoxygenases (A review)"J Lipid Med and Cell Signal. 68-69. 245-262 (2002)▼

[Publications] Zhu H., Takahashi Y., Xu W., Kawajiri H., Murakami T., Yamamoto M., Iseki S., Iwasaki T., Hattori H. and Yoshimoto T.: "Low density lipoprotein receptor-related protein-mediated membrane translocation of 12/15-lipoxygenase is required for oxidation of low density lipoprotein by macrophages"J Biol Chem. 278. 13350-13355 (2003)▼

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