

# Elucidation of physiological function of anandamide, an endogenous marijuana-like substance, in mammals

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# 2007 Fiscal Year Final Research Report Summary

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## Elucidation of physiological finction of anandamide, an endogenous marijuana-like substance, in mammals

Research Project

### Project/Area Number

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18590297

### Research Category

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Grant-in-Aid for Scientific Research (C)

### Allocation Type

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Single-year Grants

### Section

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一般

### Research Field

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Pathological medical chemistry

### Research Institution

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Kanazawa University (2007)  
Kagawa University (2006)

### Principal Investigator

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**OKAMOTO Yasuo** Kanazawa University, Graduate School of Medicine, Associate Professor (80293877)

### Co-Investigator(Kenkyū-buntansha)

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UEKI Masaaki Kagawa University, School of Medicine, Associate Professor (20213332)  
UENO Masaki Kagawa University, School of Medicine, Associate Professor (30322267)

### Project Period (FY)

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2006 – 2007

### Keywords

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N-Acylethanolamine / N-Acylphosphatidylethanolamine / Anandaroide / Endocannabinoid / Phospholipase D

### Research Abstract

N-Acylethanolamines (NAEs) constitute a large and diverse class of signaling lipids that includes the endogenous cannabinoid anandamide. It is widely accepted that in mammalian tissues all NAEs are principally released from their corresponding N-acyl phosphatidylethanolamines (NAPEs) by the catalysis by a membrane-associated phospholipase D generally abbreviated as NAPE-PLD. Recently, NAPE-PLD was identified as a candidate enzyme involved in the biosynthesis of NAEs by us. To understand the physiological and pathophysiological significance of anandamide and other bioactive NAEs in mammals, we generated and characterized mice with a targeted disruption in the NAPE-PLD gene (NAPE-PLD-1). (1) We generated mice lacking NAPE-PLD, exon 3 of the NAPE-PLD gene was removed by Cre/loxP system. (2) NAPE-PLD-1<sup>-/-</sup> were born at the expected Mendelian frequency, were viable and healthy, and showed no overt differences in their cage behavior compared to wild type littermates. (3) RT-PCR and Western blotting with anti-NAPE-PLD antibodies confirmed the absence of NAPE-PLD mRNA and protein in tissues from NAPE-PLD-1<sup>-/-</sup>. (4) Tissues from NAPE-PLD-1<sup>-/-</sup> showed significantly lower NAPE-PLD activity with an N-palmitoyl-PE as substrate compared to wild type tissues. (5) Significant reductions in the levels of saturated NAEs were observed in NAPE-PLD-1<sup>-/-</sup> brains. On the other hand, complementary profiles of NAPEs were found in NAPE-PLD<sup>+/+</sup> and NAPE-PLD-1<sup>-/-</sup> brains, with the latter samples possessing 15-20-fold higher levels of saturated N-acyl NAPEs. These data suggest that NAPE-PLD is a principal enzyme responsible for the conversion of NAPEs to NAEs in mammals.

## Research Products (56 results)

	All	2008	2007	2006	Other
	All	Journal Article (16 results) (of which Peer Reviewed: 8 results)			
		Presentation (40 results)			
[Journal Article] The expression of osteopontin is increased in vessels with blood-brain barrier impairment		2008	▼		
[Journal Article] The stimulatory effect of phosphatidylethanolamine on N-acylphosphatidylethanolamine-hydrolyzing phospholipase D (NAPE-PLD).		2008	▼		
[Journal Article] The expression of osteopontin is increased in vessels with blood-brain barrier impairment		2008	▼		
[Journal Article] The stimulatory effect of phosphatidylethanolamine on N-acylphosphatidylethanolamine-hydrolyzing phospholipase D (NAPE-PLD)1		2008	▼		
[Journal Article] Discovery and characterization of a Ca <sup>2+</sup> -independent phosphatidylethanolamine N-acyltransferase generating the anandamide precursor and its congeners		2007	▼		
[Journal Article] Proteolytic activation and glycosylation of N-acylethanolamine-hydrolyzing acid amidase, a lysosomal enzyme involved in the endocannabinoid metabolism.		2007	▼		
[Journal Article] Biosynthetic pathways of the endocannabinoid anandamide.		2007	▼		
[Journal Article] Predominant expression of lysosomal N-acylethanolamine-hydrolyzing acid amidase in macrophages revealed by immunochemical studies.		2007	▼		
[Journal Article] Accumulation of triosephosphate isomerase, with sequence homology to Beta amyloid peptides, in vessel walls of the newborn piglet hippocampus.		2007	▼		
[Journal Article] Discovery and characterization of a Ca <sup>2+</sup> -independent phosphatidylethanolamine N-acyltransferase generating the anandamide precursor and its congeners		2007	▼		
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[Journal Article] Accumulation of triosephosphate isomerase, with sequence homology to Beta amyloid peptides, in vessel walls of the newborn Piglet hippocampus		2007	▼		
[Journal Article] Functional analysis of the purified anandamide-generating phospholipase D as a member of the metallo-β-lactamase family		2006	▼		
[Journal Article] Functional analysis of the purified anandamide -generating phospholipase D as a member of the metallo-B-lactamase family		2006	▼		

[Presentation] レシチン・レチノール・アシル転移酵素構造類似タンパク質のホスファチジルエタノールアミンN-アシル転移酵素としての同定	2007	▼
[Presentation] 生体膜成分とリン脂質によるN-アシルホスファチジルエタノールアミン水解ホスホリパーゼD (NAPE-PLD)の活性化	2007	▼
[Presentation] N-アシルエタノールアミン水解酸性アミダーゼの免疫化学的解析	2007	▼
[Presentation] Identification of the protein with a homology to lecithin-retinol acyltransferase as phosphatidylethanolamine N-acyltransferase	2007	▼
[Presentation] Activation of N-acylphosphatidylethanolamine-hydrolyzing phospholipase D (NAPE-PLD) by membrane lipids and phosphatidylethanolamine	2007	▼
[Presentation] Immunocheraical studies of N-acylethanolamine -hydrolyzing acid amidase	2007	▼
[Presentation] 抗炎症脂質N-アシルエタノールアミンを加水分解する酸性アミダーゼのマクロファージにおける発現	2007	▼
[Presentation] Discovery of a calcium-independent phosphatidylethanolamine N-acyltransferase	2007	▼
[Presentation] Immunochemical studies reveal predominant expression of lysosomal N-acylethanolamine-hydrolyzing acid amidase in macrophages	2007	▼
[Presentation] Discovery of a calcium-independent phosphatidylethanolamine N-acyltransferase (iNAT)	2007	▼
[Presentation] N-アシルPEを生成する新規N-アシル転移酵素の同定と性状解析	2007	▼
[Presentation] Identification and characterization of a novel phosphatidylethanolamine Nacyltransferase generating N-acylphosphatidylethanolamine	2007	▼
[Presentation] 内因性マリファナ様物質アナンダミドの生合成に係わる新規N-アシル転移酵素の同定と性状解析	2007	▼
[Presentation] Identification and characterization of a phosphatidylethanolamine N-acyltransferase generating the anandamide an endogenous marijuana-like substance	2007	▼
[Presentation] 新規リソソーム酵素としてのN-アシルエタノールアミン水解酸性アミダーゼの性状解析	2007	▼
[Presentation] Characteization of N-acylethanolamine -hydrolyzing acid amidase as a novel lysosomal enzyme	2007	▼
[Presentation] アナンダミド前駆体N-アシルホスファチジルエタノールアミンのマクロファージ貪食抑制効果	2007	▼
[Presentation] Inhibitory effect of N-acylphosphatidylethanolamine on macrophage phagocytosis	2007	▼
[Presentation] レシチン・レチノール・アシルトランスフェラーゼにホモロジーを示す機能未知のタンパク質はホスファチジルエタノールアミンN-アシルトランスフェラーゼとして作用する	2007	▼
[Presentation] The protein with a homology to lecithin-retinol acyltransferase functions as a phosphatidylethanolamine N-acyltransferase	2007	▼
[Presentation] Expression analysis of N-acylethanolamine-generating phospholipase D in rat brain	2006	▼
[Presentation] Molecular. cloning and characterization of a novel lysosomal enzyme hydrolyzing anandamide and other bioactive N-acylethanolamines	2006	▼
[Presentation] Molecular.cloning and characterization of a novel lysosomal enzyme hydrolyzing anandamide and other bioactive N-acylethanolamines	2006	▼
[Presentation] マクロファージにおける酸性アミダーゼによる抗炎症脂質N-アシルエタノールアミンの加水分解	2006	▼
[Presentation] Purification and characterization of recombinant NAPE-PLD expressed in Escherichiacoli	2006	▼
[Presentation] Purification and characterization of recombinant NAPE-PLD expressed in Escherichia coli	2006	▼

[Presentation] Molecular. characterization of a novel lysosomal enzyme hydrolyzing anandamide and other bioactive N-acylethanolamines	2006	▼
[Presentation] Purification and characterization of the recombinant anandamide-generating phospholipase D	2006	▼
[Presentation] Molecular.characterization of a novel lysosomal enzyme hydrolyzing anandamide and other bioactive Nacylethanolamines	2006	▼
[Presentation] Purification and characterization of the recombinant anandamide-generating phospholipase D	2006	▼
[Presentation] アナンドミドを含むN-アシルエタノールアミンを遊離する新規ホスホリパーゼDの組換え酵素の大腸菌からの精製と性状解析	2006	▼
[Presentation] Purification and characterization of the recombinant enzyme of a novel phospholipase D releasing anadamide and other N-acylethanolamine from Escherichia coli	2006	▼
[Presentation] アナンドミドを遊離する新規ホスホリパーゼDの組換え体の精製と性状解析	2006	▼
[Presentation] Molecular biological studies on the anandamide-generating phospholipase D(NAPE-PLD)	2006	▼
[Presentation] N-アシルホスファチジルエタノールアミンを特異的に加水分解するホスホリパーゼD(NAPE-PLD)の組換え酵素の性状解析・	2006	▼
[Presentation] Purification and characterization of the recombinant enzyme of a novel phospholipase D releasing anadamide	2006	▼
[Presentation] Molecular biological studies on the anandamide-generating phospholipase D (NAPE-PLD)	2006	▼
[Presentation] Characterization of the recombinant N-acylphoshatidyletanolamine-hydrolyzing phospholipase D (NAPE-PLD)	2006	▼
[Presentation] Expression of anti-inflammatory lipid N-acylethanolamine -hydrolyzing acid amidase in macrophages		▼
[Presentation] Hydrolysis of anti-inflammatory lipid N-acylethanolamine by acid amidase in macrophages		▼

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