Characterization of Mouse Cysteinyl Leukotriene Receptors 
mCysLT₁ and mCysLT₂
DIFFERENTIAL PHARMACOLOGICAL PROPERTIES AND TISSUE DISTRIBUTION

Received for publication, October 1, 2001, and in revised form, February 15, 2002
Published, JBC Papers in Press, February 19, 2002, DOI 10.1074/jbc.M109447200

Cysteinyl leukotrienes (LTs) are important proinflammatory mediators. Their precise roles in mice need to be elucidated to interpret mouse models of inflammatory diseases. For this purpose, we cloned and characterized mouse receptors for cysteinyl LTs, mCysLT₁ and mCysLT₂. mCysLT₁ and mCysLT₂ were composed of 339 amino acids with 87.4% identity and 36% amino acids with 73.4% identity to human orthologues, respectively. A pharmacological difference was noted between mouse and human CysLT₁, antagonized mCysLT₂ responses as determined by Ca²⁺ elevation and receptor-induced promoter activation. The mRNA expressions of both mCysLT₁ were higher in C57BL/6 mice than in 129 mice. mCysLT₂ mRNA was expressed mainly in skin, lung, and small intestine. mCysLT₂ was seen more ubiquitously with high expressions in spleen, lung, and small intestine. By in situ hybridization we demonstrated for the first time that mCysLT₁ and mCysLT₂ were expressed in subcutaneous fibroblasts. The different pharmacological characteristics of CysLT₂ between human and mouse and the different distributions of CysLTs between mouse strains suggest that careful choice and interpretation are necessary for a study of CysLTs using animal models.

Cysteinyl leukotrienes (LTs)⁴ including LTC₄, LTD₄, and LTE₄ are inflammatory mediators previously known as SRS-A (slow reacting substances of anaphylaxis) (1–4). They are produced by LTC₄ synthase from the biologically inactive precursor LTA₄, a product of 5-lipoxygenation of arachidonic acid (5–7). LTC₄ synthase is expressed in inflammatory cells including mast cells, eosinophils, basophils, and monocytes/macrophages (7). The cysteinyl LTs are potent bronchoconstrictors and macrophage activators, and have been identified in urine and tissues in asthmatic patients (8–10). At least two cysteinyl LT receptors (CysLT₁ and CysLT₂) have been defined pharmacologically as G protein-coupled receptors. Most of the biological reactions of cysteinyl LTs including bronchospasm, plasma exudation, vasoconstriction, mucus secretion, and eosinophil recruitment are mediated through interaction with CysLT₁ (11). CysLT₁ antagonists, montelukast (Singulair™) (12, 13), zafirlukast (Accolate™) (14), and pranlukast (Onon™) (15) are currently used clinically for the treatment of bronchial asthma and allergic rhinitis. Human CysLT₁, human CysLT₂, and mouse CysLT₁ were recently cloned and characterized (16–21). Human CysLT₂ mRNA was detected in airway smooth muscle cells, tissue macrophages, monocytes, and eosinophils (16, 17). Human CysLT₂ mRNA was prominently expressed in lung macrophages, airway smooth muscle, cardiac Purkinje cells, adrenal medulla cells, peripheral blood leukocytes, placenta, spleen, and brain (18–20).

Ovalbumin sensitization and aerosol challenge in mice elicits release of LTD₄ and LTE₄ into bronchoalveolar lavage fluid, eosinophilia in the mucosa and the bronchoalveolar lavage fluid, and increased airway reactivity to methacholine (22). Although cysteinyl LTs are not established as bronchconstrictors in mice, MK-571, a CysLT₁-selective antagonist, inhibits eosinophilia, bronchial hyperreactivity, and microvascular leakage of mice (23), suggesting a contribution of cysteinyl LTs in these processes. We cloned and characterized the mouse Cys LT₁ (mCysLT₁) and Cys LT₂ (mCysLT₂) to better study the roles of cysteinyl LTs in animal models of diseases.

MATERIALS AND METHODS

Antagonists—Pranlukast was a generous gift from Ono Pharmaceutical Co. (Osaka, Japan). MK-571 and BAY u9773 were purchased from BIOMOL Research Laboratories (Plymouth Meeting, PA). Pranlukast and MK-571 were dissolved in 100% ethanol to make 10 mM stock solutions.

Cloning and Expression of mCysLT₁ and mCysLT₂—A mouse genome library (129 inbred strain) in AfxII vector (Stratagene, La Jolla, CA) was screened with low-³²PIdCTP-labeled partial open reading frame (ORF) of human CysLT₁ (581 nucleotides), and a clone was isolated. The CysLT₁ ORF from C57BL/6 was obtained by PCR with a genome template using sense (5’-ATCCCTGGAGAACATGAATGG-3’ and antisense (5’-CATTGTTCTGCACTGTAGATGAG-3’) primers. A mouse expressed sequence tag clone with 88.4% identity in cDNA sequence to the human CysLT₁ was found during a routine BLAST search of the NCBI data base (GenBank™ accession number AI506060), and it was purchased from Genome Systems (St. Louis, MO). These three clones were sequenced using an automated DNA sequencer 373A (Applied Biosystems, Foster City, CA) and found to be completely identical. The ORF of the expressed sequence tag clone was amplified by PCR with

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* The work was supported in part by Grants-in-aid from the Ministry of Education, Culture, Sports and Science of Japan and grants from the Yamashita Foundation for Metabolic Disorders and the Ono Medical Research Foundation. The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

The nucleotide sequence(s) reported in this paper has been submitted to the GenBank™ ERD Data Bank with accession number(s) AB044087 and AB058390.

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‡ The abbreviations used are: LT, leukotriene; CHO, Chinese hamster ovary; FCS, fetal calf serum; GSPDH, glyceraldehyde-3-phosphate dehydrogenase; HEK, human embryonic kidney; ORF, open reading frame; PBS, phosphate-buffered saline; m, mouse; AM, aceotxyethyl; TM, transmembrane domain.
sense (5'-CCGGGATCCCGAATGAACTGAAAATCTGAC-3') and antisense (5'-GCTTCTAGATTTCACTGATTTCTT-3') primers, subcloned into a pGEM-T Easy Vector (Promega, Madison, WI), digested with restriction enzymes (BanHI and XbaI), and subcloned again into an expression vector, pcDNA4HisMax (Invitrogen, Carlsbad, CA) to obtain pc4HM-mCysLT1. For the cloning of a mouse CysLT2 orthologue, the mouse genomic library in a FIXII vector was screened by plaque hybridization using [α-32P]dCTP-labeled full-length ORF of human CysLT2 cDNA (19) as a probe. The fragments that hybridized to the mouse CysLT2 cDNA (19) as a probe. The fragments that hybridized to the mouse CysLT2 cDNA were sequenced as described above. The putative ORF was attached with an hemagglutinin tag at its N terminus and subcloned into an expression vector pcDNA3.1 (Invitrogen) between the BamHI and XbaI sites to obtain pc3.1-mCysLT2. The CysLT2 ORF from C57BL/6 was obtained by PCR with a genome template using primers designed from the 129 genome sequence.

Cell Culture and Transfection—HEK-293 cells and B103 cells were cultured in Dulbecco's modified Eagle's medium (Sigma) supplemented with 10% fetal calf serum (FCS; Sigma), 100 IU/ml penicillin, and 100 μg/ml streptomycin; PC12 cells in Dulbecco's modified Eagle's medium supplemented with 10% horse serum, 10% FCS, 100 IU/ml penicillin, and 100 μg/ml streptomycin; CHO cells in Nutrient Mixture F-12 Medium (Sigma) supplemented with 10% FCS, 100 IU/ml penicillin, and 100 μg/ml streptomycin; and CHO cells in Nutrient Mixture F-12 Medium (Sigma) supplemented with 10% FCS, 100 IU/ml penicillin, and 100 μg/ml streptomycin.

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Fig. 1. Amino acid sequence of mCysLT1 and mCysLT2. A, structures of mCysLT1 and mCysLT2 are shown. The putative transmembrane segments I–VII of mCysLT1 and mCysLT2 are underlined. The asterisks indicate identical amino acids, and dots indicate similar amino acids. B, amino acid identities between mCysLT1, mCysLT2, human CysLT1, and human CysLT2 are shown. AA, amino acids.
and Renilla luciferase values were measured using PICAGENE Dual Seapansy and a Mini Lumat LB9506 luminometer (Berthold, Bad Wilsensc, Germany). Firefly luciferase values were standardized to Renilla values.

**Northern Blotting**—Total RNA was extracted from 129+ TerSw Jcl (Clea Japan, Tokyo, Japan) and C57BL/6 Jcl (Clea Japan) mouse tissues including brain, heart, lung, liver, spleen, kidney, small intestine, skeletal muscle, and skin, using Isogen (Wako, Osaka, Japan). Poly(A)+ RNA was isolated from 200 μg of the total RNA using a μMACS mRNA isolation kit (Miltenyi Biotec, Bergisch Gladbach, Germany). The RNA samples were denatured, electrophoresed on 0.7% formaldehyde-agarose gels, and transferred onto nylon membranes Hybond-N+ (Amersham Biosciences) as described (26). The membranes were hybridized with [α-32P]dCTP-labeled ORF of mCysLT1, pc3.1-mCysLT2, and an expressed sequence tag clone containing mG3PDH cDNA (GenBank™ accession number BF537941) purchased from IncyteGenomics (Palo Alto, CA) were used as standards. Primers were chosen so that they would yield PCR products identical in DNA sequence from 129 and C57BL/6 inbred strains. The following primers were used: mCys1-760-5'-CTTGCTCAGTGTCCTTGCTG-3'; mCys2-662-5'-AGGTTGTCTCCTGCGACTTC-3'; mCys2-843-5'-AGCCTTCTCCTAAAGTTTCCAC-3'; mCys3-923-5'-CCATGGTC-3'; mCys1-923-5'-GTCCACGTGCTGCTCATAGG-3'; mG3PDH-1089-5'-CAGGCCATCGTGCCTCTGT-3'; mG3PDH-879-5'-CCATGGTC-3'; mCys2-843-5'-AGCCTTCTCCTAAAGTTTCCAC-3'. These primer pairs result in PCR products of 164 (mCysLT1), 182 (mCysLT2), and 211 bp (G3PDH). The standards and the samples were simultaneously amplified using the same reaction master mixture. The reactions were incubated at 95°C for 10 min to activate the polymerase, followed by 50 cycles of amplification. Each cycle of PCR included 3 s of denaturation at 95°C, 3 s of primer annealing at 67°C for G3PDH, 65°C for mCysLT1, and 68°C for mCysLT2, and 10 s of extension at 72°C. The temperature ramp was 20°C/s. At the end of the extension steps, the fluorescence of each sample was measured to allow quantification of the CDNs. After cycling, melting curves of the PCR products were acquired by stepwise increase of the temperature from 5°C above the annealing temperature to 95°C. Using LightCycler analysis software, the SYBR Green I signal of each sample was plotted versus the

**Products of Mouse Cysteinyl Leukotriene Receptors**—Total RNA was prepared as described above from 129 and C57BL/6 mouse adrenal gland, peritoneal macrophages, and spleen. For elicitation of peritoneal macrophages, the animals were injected with 2 ml of 4% thioglycollate broth 4 days prior to sacrifice and peritoneal lavage using ice-cold PBS with 2 mM EDTA. cDNA was synthesized from 1 μg of total RNA using Superscript II (Invitrogen) and 50 ng of random hexamers according to the manufacturer’s protocol, and 2 μl of the cDNA was diluted in 38 μl of 10 mM Tris-HCl, 1 mM EDTA (pH 8.0) for PCR. PCR was carried out using a LightCycler System (Roche Molecular Biochemicals), and the

**Quantitative Real Time Reverse Transcriptase-PCR**—Total RNA was synthesized from 1 μg of total RNA using Superscript II (Invitrogen) and 50 ng of random hexamers according to the manufacturer’s protocol, and 2 μl of the cDNA was diluted in 38 μl of 10 mM Tris-HCl, 1 mM EDTA (pH 8.0) for PCR. PCR was carried out using a LightCycler System (Roche Molecular Biochemicals), and the

**FIG. 2.** Ca2+ response and reporter gene expression using mCysLT2. A and B, Ca2+ mobilization in HEK-293 cells stably expressing mCysLT2. A, the mCysLT2-expressing cells (HEK 7-1) loaded with Fura2-AM were challenged with 100 nM LTD4 (open arrow), and the change in [Ca2+]i was measured. The right panel shows the response of the cells treated with 10 μM pranlukast 5 min before the challenge. The results are representative of three independent experiments. B, HEK 7-1 cells were loaded with Fura2-AM and stimulated with various concentrations of LTC4 or LTD4. Vector-transfected HEK-293 cells stimulated with LTC4 or LTD4 were used as negative controls. The differences of [Ca2+]i before and after the challenges are shown (n = 3, means ± S.E.). Statistically significant differences between the vector control and HEK 7-1 are indicated. *, p < 0.01, unpaired t test. C and D, reporter gene assays of B103 cells transiently transfected with mCysLT1 or vector alone. C, Cells transfected with mCysLT1 or vector alone were stimulated with various concentrations of LTD4. The data are expressed as fold activation over control (without LTD4) and expressed as the means ± S.E. (n = 3). Statistically significant differences between the control and the LT-stimulated cells are indicated. *, p < 0.05, unpaired t test. D, the effects of two CysLT1 antagonists are shown. The data are expressed as fold activation over the control (without LTD4) and expressed as the means ± S.E. (n = 4). Statistically significant differences between the control and the drug-treated cells are indicated. *, p < 0.05, Bonferroni’s multiple t test.
number of cycles, and the crossing points were obtained. These crossing points correlate inversely with the log of the initial template concentration. The levels of mRNA were estimated by subtracting the initial levels of target DNA in PCR reactions without reverse transcription, which represents genomic contamination. Then the mRNA levels were normalized to the level of G3PDH mRNA.

**In Situ Hybridization**—Paraffin sections of the skin samples from 129 and C57BL/6 mice fixed in 10% formalin were investigated as described previously (27, 28) by using a slightly modified nonradioactive *in situ* hybridization technique with digoxigenin-labeled RNA probes. Briefly, paraffin-embedded tissues were cut to 4-μm-thick sections, mounted onto silane-coated slides, deparaffinized, and treated with proteinase K (5 μg/ml in PBS) for 10 min at 24 °C. Then the sections were acetylated with acetic anhydride (1 ml in 400 ml of 0.1 M triethanolamine, pH 8.0) for 15 min at 24 °C. After washing with PBS, the samples were soaked in 2× SSC with 50% formamide, subjected to hybridization. Fragments of cDNAs for mCysLTs (mCysLT ORF at 687–887 and mCysLT2 ORF at 18–222) were amplified by PCR using upstream primers with a recognition sequence for HindIII and downstream primers with a recognition sequence for EcoRI, and subcloned into pSPT18 by directional cloning. The plasmids were linearized using EcoRI and downstream primers with a recognition sequence for HindIII and subcloned into pSPT18 by directional cloning. The plasmids were linearized using EcoRI and downstream primers with a recognition sequence for HindIII and subcloned into pSPT18 by directional cloning. The plasmids were linearized using EcoRI and downstream primers with a recognition sequence for HindIII and subcloned into pSPT18 by directional cloning. The plasmids were linearized using EcoRI and downstream primers with a recognition sequence for HindIII and subcloned into pSPT18 by directional cloning. The plasmids were linearized using EcoRI and downstream primers with a recognition sequence for HindIII and subcloned into pSPT18 by directional cloning.

The experiments using LTC4 were performed in the presence of 5 mM serine and 10 mM borate.

![Diagram](image_url)

**Fig. 3.** Ca2+ response and reporter gene expression using mCysLT2. A and B, Ca2+ mobilization in CHO cells stably expressing mCysLT2. The cells were loaded with Fura2-AM and challenged with LTC4 or LTD4. The increase in [Ca2+]c was calculated from the fluorescence ratio (340 nm/380 nm). A, [Ca2+]c increases of mCysLT2-expressing cells (CHO-7A1) challenged with LTC4 (■) or LTD4 (●) and vector control cells challenged with LTC4 (□) or LTD4 (○) are shown (n = 3, means ± S.E.). Statistically significant differences between the control and CHO-7A1 are indicated. *p < 0.01, unpaired *t* test. B, effects of CysLT antagonists were examined. The increase in [Ca2+]c after 100 nM LTC4 stimulation is shown as a percentage to that of the cells without an antagonist (n = 2, each replicate shown). BAY u9773 (■) and pranlukast (●) inhibited the response to LTC4, whereas MK-571 (□) did not affect the response to the LTC4 stimulation. Neither MK-571, pranlukast, nor BAY u9773 affected Ca2+ response and reporter gene expression using mCysLT2.

**C.** The digoxigenin-labeled antisense probes and EcoRI restriction sequence for mCysLT2 were performed in the presence of 5 mM serine and 10 mM borate. D, the responses to 10 nM LTD4 in the presence of various concentrations of MK-571 (▲), pranlukast (●), or BAY u9773 (■) are shown (n = 2, each replicate shown).

**RESULTS AND DISCUSSION**

The Structure of mCysLT1 and mCysLT2—mCysLT1 and mCysLT2 were predicted to be polypeptides of 339 and 309 amino acid residues, respectively (Fig. 1A). The identities of the amino acid sequences between 129 mouse and human (16–18) CysLTs are shown in Fig. 1B. mCysLT1 was longer than human CysLT1 by two amino acid residues. mCysLT2 was shorter than human CysLT2 by 37 amino acid residues, being truncated at both the N and C termini. The sequence of mCysLT1 was identical among 129, C57BL/6, and BALB/c mice, and there was a mismatch in mCysLT2 sequences at the 213th amino acid residue between 129 (Val) and C57BL/6 (Ile). The preserved amino acids in the rhodopsin-like G protein-coupled
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Pharmacological Properties of mCysLT 1 and mCysLT 2—Mouse orthologues of CysLT 1 and CysLT 2 were identified as functional cysteinyl LT receptors by several methods. CysLT 1 and CysLT 2 are known to increase $[Ca^{2+}]_i$ and CysLT 2 is known to increase $[Ca^{2+}]_i$ in HEK-293 cell lines stably expressing mCysLT 1 (HEK 7-1) and mCysLT 2 (HEK 7-3) (data not shown). LTC 4 also evoked a slight increase in $[Ca^{2+}]_i$, (Fig. 2B), whereas LTD 4 or LTE 4 did not (data not shown). These cells pretreated with a CysLT 1 antagonist, pranlukast (Fig. 2A) or MK-571 (data not shown), did not respond to LTD 4, whereas they remained responsive to ATP. In reporter gene assay, B103 cells transiently expressing mCysLT 1 increased luciferase activity in response to LTD 4 in a dose-dependent manner but was not inhibited by a CysLT 1-specific antagonist, MK-571 (Fig. 3B). The response of CHO-883 cells, another mCysLT 2-expressing clone, was similar to that of CHO-7A1 (n = 3; data not shown). ATP (10 μM) elicited the same level of increase in $[Ca^{2+}]_i$ in CHO-7A1, CHO-883, and the vector control (n = 3; data not shown). PC12 cells transiently expressing mCysLT 2 increased luciferase activities in response to LTC 4 and LTD 4 to the same extent in dose-dependent manners (Fig. 3C), and the responses were inhibited by BAY u9773 and not by MK-571 (Fig. 3D). Surprisingly, pranlukast, found to be a CysLT 1-specific antagonist from human studies (16, 17), inhibited the LTC 4-induced increase in $[Ca^{2+}]_i$ (Fig. 3B) and the LTD 4-induced luciferase activity (Fig. 3D) in the cells expressing mCysLT 2. Several reports showing that pranlukast does not antagonize human CysLT 2 (18, 20) imply a pharmacological difference of CysLT 2 between human and mouse likely because of significant difference in primary structure (Fig. 1B). BAY u9773 was partially agonistic on mCysLT 2 as is reported in human CysLT 2 (19) (data not shown).

Different Tissue Distribution of CysLT 1 and CysLT 2 mRNA in Two Mouse Inbred Strains—Hybridization of poly(A) + RNA from various mouse tissues detected transcripts of 3.0 and 5.5 kb for CysLT 1 and CysLT 2, respectively (Fig. 4A). As a whole, the expression levels of CysLTs were higher in C57BL/6 inbred strain than in 129 inbred strain, even though a slight difference in control hybridization (G3PDH) in Northern blotting was observed in some tissues. In C57BL/6 strain, the highest mRNA expression for CysLT 1 was observed in skin, lung, small intestine, and macrophages, and moderate expressions were found in other tissues; the expression of CysLT 2 was ubiquitous with higher expressions in spleen, lung, and small intestine (Fig. 4). Differential tissue expression between two strains suggests that regulatory polymorphism is present.

Given the importance of cysteinyl LTs in skin diseases including atopic dermatitis (31), we investigated the distribution of CysLTs in mouse skin by in situ hybridization. We chose 129 inbred strain because Goulet et al. (32) had reported the potent inflammatory response of the skin in 129 mice. No signals of either LTB 4 or LTE 4 at a concentration of 10 or 100 nM (data not shown). The LTD 4-induced response was inhibited by pranlukast or MK-571 (Fig. 2D).

In CHO cells stably expressing mCysLT 2 (CHO-7A1), LTC 4 and LTD 4 exhibited dose-dependent increases in $[Ca^{2+}]_i$ (Fig. 3A). The response was inhibited by BAY u9773, a nonselective antagonist of cysteinyl LT receptors (30), in a dose-dependent manner but was not inhibited by a CysLT 1-specific antagonist, MK-571 (Fig. 3B). The response of CHO-883 cells, another mCysLT 2-expressing clone, was similar to that of CHO-7A1 (n = 3; data not shown). ATP (10 μM) elicited the same level of increase in $[Ca^{2+}]_i$ in CHO-7A1, CHO-883, and the vector control (n = 3; data not shown). PC12 cells transiently expressing mCysLT 2 increased luciferase activities in response to LTC 4 and LTD 4 to the same extent in dose-dependent manners (Fig. 3C), and the responses were inhibited by BAY u9773 and not by MK-571 (Fig. 3D). Surprisingly, pranlukast, found to be a CysLT 1-specific antagonist from human studies (16, 17), inhibited the LTC 4-induced increase in $[Ca^{2+}]_i$ (Fig. 3B) and the LTD 4-induced luciferase activity (Fig. 3D) in the cells expressing mCysLT 2. Several reports showing that pranlukast does not antagonize human CysLT 2 (18, 20) imply a pharmacological difference of CysLT 2 between human and mouse likely because of significant difference in primary structure (Fig. 1B). BAY u9773 was partially agonistic on mCysLT 2 as is reported in human CysLT 2 (19) (data not shown).
CysLTs were detected in epidermis (data not shown). In the subcutaneous connective tissues, however, high expressions of CysLT$_1$ (Fig. 5a) and CysLT$_2$ mRNA (Fig. 5c) were seen mostly in fibroblasts. No signal was obtained using the sense control (Fig. 5, b and d). It has been reported that cysteinyll LTs increase collagen synthesis in fibroblasts (33, 34), and our report is the first to demonstrate the expression of CysLTs in fibroblasts. Further study is needed to uncover yet unknown roles of cysteinyl LTs in wound healing and pathological collagen synthesis.

In conclusion, we have cloned mCysLT$_1$ and mCysLT$_2$ and found differences in the pharmacological characteristics between mouse and human CysLT$_2$. There are differences in mRNA expression of CysLT$_1$ and CysLT$_2$ between mouse strains, suggesting the importance of choosing a proper mouse strain for a disease model. We also discovered expression of both CysLTs in subcutaneous fibroblasts. These data are useful in interpreting and understanding the physiological and pathological roles of CysLTs in animal models of human diseases.

Acknowledgments—We thank Drs. D. A. Wong, S. Sato, and K. Kishimoto for suggestions and M. Ito for technical assistance.

REFERENCES

1. Murphy, R. C., Hammarstrom, S., and Samuelsson, B. (1979) Proc. Natl. Acad. Sci. U. S. A. 76, 4275–4279
2. Shimizu, T., and Wolfe, L. S. (1990) J. Neurochem. 55, 1–15
3. Samuelsson, B. (1983) Science 219, 568–575
4. Samuelsson, B., Dahlen, S. E., Hammarstrom, S., and Samuelsson, B. (1980) Proc. Natl. Acad. Sci. U. S. A. 77, 645–650
5. Welsch, D. J., Creely, D. P., Hauser, S. D., Mathis, K. J., Krivi, G. G., and Isakson, P. C. (1994) Proc. Natl. Acad. Sci. U. S. A. 91, 9745–9749
6. Lam, B. K. (1997) Proct. Bional. 2, 380–386
7. Penrose, J. F., and Austen, K. F. (1999) Proc. Assoc. Am. Physicians 111, 537–546
8. Dahlen, S. E., Hedqvist, P., Hammarstrom, S., and Samuelsson, B. (1989) Nature 338, 484–486
9. Piper, P. J. (1984) Physiol. Rev. 64, 744–761
10. Lewis, R. A., Austen, K. F., and Soberman, R. J. (1990) N. Engl. J. Med. 323, 645–655
11. Drazen, J. M. (1998) Am. J. Respir. Crit. Care Med. 158, (suppl.) 193–200
12. Jones, T. R., Labelle, M., Belley, M., Champion, E., Charette, L., Evans, J., Ford-Hutchinson, A. W., Gauthier, J. Y., Lord, A., Masson, P., McFarlane, C. S., Piechuta, H., Rokach, J., Williams, H., and Young, R. N. (1989) Can. J. Physiol. Pharmacol. 67, 17–28
13. Obata, T., Okada, Y., Motoishi, M., Nakagawa, N., Terawaki, T., and Aishita, H. (1992) Ypn. J. Pharmacol. 60, 227–237
14. Lynch, K. R., O’Neill, G. P., Liu, Q., Im, D. S., Sawyer, N., Metters, K. M., Coulomb, N., Abramowitz, M., Figueroa, D. J., Zeng, Z., Connolly, B. M., Bai, C., Austin, C. P., Chateauneuf, A., Stocco, R., Greig, M. G., Karmann, S., Hooks, S. B., Hosfield, E., Williams, D. L., Jr., Ford-Hutchinson, A. W., Caskey, C. T., and Evans, J. F. (1999) Nature 399, 789–793
15. Sarau, H. M., Ames, R. S., Chambers, J., Ellis, C., Elshourbagy, N., Feiley, J. J., Schmidt, D. B., Macciuelli, R. M., Jenkins, O., Mordock, P. R., Herrity, N. C., Halsey, W., Sathe, G., Mair, A. I., Nuthalaganti, P., Dyrko, G. M., Buckley, P. T., Wilson, S., Bergsma, D. J., and Hay, D. W. (1999) Mol. Pharmacol. 56, 657–663
16. Heise, C. E., O’Dowd, B. F., Figueroa, D. J., Sawyer, N., Nguyen, T., Im, D. S., Stocco, R., Bellefeuille, J. N., Abramowitz, M., Cheng, R., Williams, D. L., Jr., Zeng, Z., Liu, Q., Ma, L., Clements, M. K., Coulombe, N., Liu, Y., Austin, C. P., George, S. R., O’Neill, G. P., Metters, K. M., Lynch, K. R., and Evans, J. F. (2000) J. Biol. Chem. 275, 30531–30536
17. Nothacker, H. P., Wang, Z., Zhu, Y., Reinscheid, R. K., Lin, S. H., and Civeilli, O. (2000) Mol. Pharmacol. 58, 1601–1608
18. Takasaki, J., Kamohara, M., Matsumoto, M., Saito, T., Sugimoto, T., Okoshi, T., Ishii, H., Ota, T., Nishikawa, T., Kawai, Y., Mausho, Y., Isogai, T., Suzuki, Y., Sugano, S., and Furuiuchi, K. (2000) Biochem. Biophys. Res. Commun. 274, 316–322
19. Maekawa, A., Kanaoka, Y., Lam, B. K., and Austen, K. F. (2001) Proc. Natl. Acad. Sci. U. S. A. 98, 2256–2261
20. Henderson, W. R., Jr., Lewis, D. B., Albert, R. K., Zhang, Y., Lamm, W. W., Chiang, C. R., Jones, F., Eriksen, P., Tien, Y. T., Jonas, M., and Chi, E. Y. (1999) J. Exp. Med. 184, 1485–1494
21. Jones, T. R., Zamboni, R., Belley, M., Champion, E., Charette, L., Ford-Hutchinson, A. W., Frenette, R., Gauthier, J. Y., Leger, S., Masson, P., McFarlane, C. S., Piechuta, H., Rokach, J., Williams, H., and Young, R. N. (1999) Can. J. Physiol. Pharmacol. 67, 17–28
22. Yamazawa, T., Iino, M., and Endo, M. (1992) FEBS Lett. 301, 181–184
23. Kawasawa, Y., Kume, K., Isumi, T., and Shimizu, T. (2000) Biochem. Biophys. Res. Commun. 276, 557–564
24. Chomczynski, P. (1992) Anal. Biochem. 201, 134–139
25. Igarashi, A., Nishino, K., Kikuchi, K., Sato, S., Ihn, H., Fujimoto, M., Grotendorst, G. R., and Takehara, K. (1999) J. Invest. Dermatol. 106, 729–733
26. Igarashi, A., Nishino, K., Kikuchi, K., Sato, S., Ihn, H., Grotendorst, G. R., and Takehara, K. (1995) J. Invest. Dermatol. 105, 280–284
27. Chan, C. C., Eccleston, P., Nicholson, D. W., Metters, K. M., Pen, D. J., and Rodger, I. W. (1994) J. Pharmacol. Exp. Ther. 269, 891–896
28. Coleman, R. A., Eglen, R. M., Jones, R. L., Narumiya, S., Shimizu, T., Smith, W. L., Dahlen, S. E., Draven, J. M., Gardiner, P. J., Jackson, W. T., Jones, T. R., Krell, R. D., and Nicollia, S. (1996) Adv. Prostaglandin Thromboxane. Leukot. Res. 23, 283–285
29. Hishinuma, T., Suzuki, N., Aiba, S., Tagami, H., and Mizugaki, M. (2001) Br. J. Dermatol. 144, 19–23
30. Goulet, J. L., Byrum, R. S., Key, M. L., Nguyen, M., Wagoner, V. A., and Koller, B. H. (2000) J. Immunol. 164, 4899–4907
31. Phan, S. H., McGarry, B. M., Leffler, K. M., and Kunkel, S. L. (1988) Biochemistry 27, 2946–2953
32. Abe, M., Kurosawa, M., Ishikawa, O., and Miyachi, Y. (2000) J. Allergy Clin. Immunol. 106, (suppl.) 78–84
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J. Biol. Chem. 2002, 277:18763-18768.
doi: 10.1074/jbc.M109447200 originally published online February 19, 2002

Access the most updated version of this article at doi: 10.1074/jbc.M109447200

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