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[Continued on next page]

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Input file Fbh25869FL.seq; Output File Fbh25869FL.tra
Sequence length 2087

ACCACCGCTCCGACGCTTGTCAACAGAGCTAGACCCCTGTCTCAAAACAAAAATAAAACAAGAAATGGGCAAGTG
CGTGCCCAAGGCAAGGCGCCCTAGTGGCCAGCCCGCTGCGCCGAGTGGAGTGGTGTAGTACTCTCAGGCAAGGCG

GGAGGAGGAAGTTGGGCGTCAACCTAAGACCAGGCTACCCGGTTGCTGGGAAGGTTACCAAG M L C G G
ATG CTG TGT GGG

P E V A Q P E V D T T L G R V R G R Q V
CCC GAA GTT GCT CAG CCT GAA GTA GAC ACC ACC CTG GGT CGT GTG CGA GGC CGG CAG GTG

G V K G T D R L V N V F L G I P F A Q P
GGC GTG AAG GGC ACA GAC CGC CTT GTG AAT GTC TTT CTG GGC ATT CCA TTT GCC CAG CCG

P L G P D R F S A P H P A Q P W E G V R
CCA CTG GGC CCT GAC CGG TTC TCA GCC CCA CAC CCA GCA CAG CCC TGG GAG GGT GTG CCG

D A S T A P P M C L Q D V E S H N S S R
GAT GCC AGC ACT GCG CCC CCA ATG TGC CTA CAA GAC GTG GAG AGC ATG AAC AGC AGC AGA

F V L N G K Q Q I F S V S E D C L V L N
TIT GTC CTC AAC GGA AAA CAG CAG ATC TTC TCC GTT TCA GAG GAC TGC CTG GTC CTC AAC

V Y S P A E V P A G S G R P V M V W V H
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G G A L I T G A A T S Y D G S A L A A Y
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G D V V V V T V Q Y R L G V L G F F S T
GGG GAT GTG GTC GTG GTT ACA GTC CAG TAC CGC CTT GGG GTC CTT GGC TTC TTC AGC ACT

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V Q E N I A P F G G D L N C V T V F G G
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S A G G S I I S G L V L S P V A A G L F
TCT GCC GGT GGG AGC ATC ATC TCT GGC CTG GTC CTG TCC CCA GTG GCT GCA GGG CTG TTC

H R A I T Q S G V I T T P G I I D S H P
CAC AGA GCC ATC ACA CAG AGT GGG GTC ATC ACC ACC CCA GGG ATC ATC GAC TCT CAC CCT

N P L A Q K I A N T L A C S S S S P A E
TGG CCC CTA GCT CAG AAA ATC GCA AAC ACC TTG GCC TGC AGC TCC AGC TCC CCG GCT GAG

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AAT NCT ATC TAT CCT CTC ACC GTT GAT GGC ACT GTC TTC CCC AAA AGC CCC AAG GAA CTC

L K E K P F H S V P F L M G V N N H E F
CTG AAG GAG AAG CCC TTC CAC TCT GTG CCC TTC CTC ATG GGT GTC AAC AAC CAT GAG TTC

S H L I P R G W G L D T H E Q H S R E
ACG TGG CTC ATC CCC AGG GGC TGG GGT CTC CTG GAT ACA ATG GAG CAG ATG AGC CCG GAG

(57) Abstract: The invention provides isolated nucleic acid molecules, designated COE-1 nucleic acid molecules, which encode novel carboxylesterase family members. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing COE-1 nucleic acid molecules, host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a COE-1 gene has been introduced or disrupted. The invention still further provides isolated COE-1 proteins, fusion proteins, antigenic peptides and anti-COE-1 antibodies. Diagnostic methods utilizing compositions of the invention are also provided.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/20968

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/55 C12N15/62 C12N9/18 C12N5/10 C12N1/21
 C12Q1/68 G01N33/53 G01N33/573

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EMBL, EPO-Internal, WPI Data, PAJ, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 00 28045 A (INCYTE PHARMA INC ;AZIMZAI YALDA (US); CORLEY NEIL C (US); YUE HEN) 18 May 2000 (2000-05-18) Note: 100.0% nt seq identity of SEQ ID NO:21 with SEQ ID NO:3 in 1633 nt overlap (119-1751:9-1641), 100.0% aa seq identity of SEQ ID NO:5 with SEQ ID NO:2 in 544 aa overlap (28-571:4-547). page 5, line 18 -page 7, line 8 table 2 claims 1-20</p> <p style="text-align: center;">--- -/--</p>	1-32

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

16 May 2002

Date of mailing of the international search report

31/05/2002

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/20968

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online! EBI; 22 February 2000 (2000-02-22) SUGANO S ET AL.: "Homo sapiens cDNA FLJ20098 fis, clone COL04537, highly similar to ESTM_MOUSE LIVER CARBOXYLESTERASE PRECURSOR" Database accession no. AK000105 XP002198768 Note: 100.0% nt seq identity with SEQ ID NO:3 in 1633 nt overlap (99-1731:9-1641). the whole document</p> <p style="text-align: center;">---</p>	1-32
X	<p>DATABASE EMBL 'Online! EBI; 4 October 1993 (1993-10-04) AIDA K ET AL.: "carboxylesterase 'mice, liver, Balb/cj X DBA/2J, mRNA, 2007 nt!" Database accession no. S64130 XP002198769 Note: 74.9% nt seq identity with SEQ ID NO:3 in 903 nt overlap (88-989:9-909). the whole document</p> <p style="text-align: center;">---</p>	5,13
A	<p>WO 99 42593 A (DANKS MARY K ;POTTER PHILIP M (US); HOUGHTON PETER J (US); ST JUDE) 26 August 1999 (1999-08-26) page 9, line 32 -page 10, line 27 example 2 figure 4</p> <p style="text-align: center;">---</p>	1,5,13
A	<p>SATOH T ET AL.: "Molecular aspects of carboxylesterase isoforms in comparison with other esterases" TOXICOLOGY LETTERS, vol. 82/83, 1995, pages 439-445, XP001053079 ISSN: 0378-4274 the whole document</p> <p style="text-align: center;">-----</p>	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 17, 19, 25, 29, 31 and 32 relate to a compound or substance defined by reference to a desirable characteristic or property, namely that it selectively binds to a polypeptide of claim 13, that it modulates the activity of a polypeptide of claim 13, that it is a COE-1 binding substance, or that it is a COE-1 modulator. The claims cover all compounds or substances having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds or substances. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds or substances by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds or substances which are antibodies or antisense molecules.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/20968

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0028045	A	18-05-2000	WO 0028045 A2	18-05-2000
			AU 1914400 A	29-05-2000
			EP 1131443 A2	12-09-2001

WO 9942593	A	26-08-1999	AU 2867999 A	06-09-1999
			CA 2320808 A1	26-08-1999
			CN 1303436 T	11-07-2001
			EP 1054979 A1	29-11-2000
			JP 2002504340 T	12-02-2002
			WO 9942593 A1	26-08-1999
