



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification<sup>6</sup> : <b>C07K 14/47, A01K 67/00</b> <b>C12N 15/12 // C12Q 1/68</b></p>	<p><b>A3</b></p>	<p>(11) International Publication Number: <b>WO 97/03192</b> (43) International Publication Date: 30 January 1997 (30.01.97)</p>											
<p>(21) International Application Number: PCT/US96/11386 (22) International Filing Date: 5 July 1996 (05.07.96)</p> <p>(30) Priority Data:</p> <table border="0"> <tr> <td>60/000,956</td> <td>7 July 1995 (07.07.95)</td> <td>US</td> </tr> <tr> <td>60/001,675</td> <td>28 July 1995 (28.07.95)</td> <td>US</td> </tr> <tr> <td>60/002,174</td> <td>11 August 1995 (11.08.95)</td> <td>US</td> </tr> <tr> <td>60/002,328</td> <td>14 August 1995 (14.08.95)</td> <td>US</td> </tr> </table> <p>(71) Applicants: DARWIN MOLECULAR CORPORATION [US/US]; 1631 220th Street S.E., Bothell, WA 98021 (US). VA MEDICAL CENTER [US/US]; Laboratory of the Department of Veterans Affairs, 1660 S. Columbian Way, Seattle, WA 98108-1597 (US). THE GENERAL HOSPITAL CORPORATION [US/US]; 55 Fruit Avenue, Boston, MA 02114 (US).</p> <p>(71)(72) Applicant and Inventor: LEVY-LAHAD, Ephrat [US/US]; 7210 - 26th Avenue Northeast, Seattle, WA 98115 (US).</p>	60/000,956	7 July 1995 (07.07.95)	US	60/001,675	28 July 1995 (28.07.95)	US	60/002,174	11 August 1995 (11.08.95)	US	60/002,328	14 August 1995 (14.08.95)	US	<p>(72) Inventors: TANZI, Rudolph, E.; 25 Strawberry Lane, Canton, MA 02021 (US). SCHELLENBERG, Gerard, D.; 7031 - 19th Avenue Northwest, Seattle, WA 98117 (US). WASCO, Wilma; 49 Sacramento Street, Cambridge, MA 02138 (US). BIRD, Thomas, D.; 16061 - 37th Avenue Northeast, Seattle, WA 98155 (US). MULLIGAN, John; 5823 - 17th Avenue N.E., Seattle, WA 98105 (US). GALAS, David, J.; 4605 Lake Washington Boulevard Southeast, Bellevue, WA 98006 (US).</p> <p>(74) Agents: McMASTERS, David, D. et al.; Seed and Berry L.L.P., 6300 Columbia Center, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).</p> <p>(81) Designated States: CA, JP, MX, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p><b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 03 April 1997 (03.04.97)</p>
60/000,956	7 July 1995 (07.07.95)	US											
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60/002,328	14 August 1995 (14.08.95)	US											

(54) Title: CHROMOSOME 1 GENE AND GENE PRODUCTS RELATED TO ALZHEIMER'S DISEASE

Protein sequence of 448 amino acids that represents the gene product of the Human AD4 gene.

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1  MLTFMADSE EEVCDERTSL MSAESPTPRS CQEGRQGPED GENTAQWRSQ
51  ENEEDGEEDP DRYVCSGVPG RPPGLEEELT LKYGAKEVIM LFVPTLCMI
101 VVATIKSVR FYTEKNGQLI YTPFTEDTFS VGQRLLSVL NTLIMISVIV
151 VMTIFLVVLY KYRCYKFIHG WLIMSSLMLL FLPTYTYLGE VLKTYNVAMD
201 YPTLLLTVMN FGAVGMVCIH WKGPLVLQQA YLIMISALMA LVFIKYLPEW
251 SANVILGAIS VYDLVAVLCP KGPLRMLVET AQERNEPIFP ALIYSSAMVW
301 TVGMKLDPS SQGALQLPYD PEMEEDSYDS FGEPSPYEVF EPPLTGYPGE
351 ELESEBERGV KLGLDGFIFY SVLVGKAAAT GSGDWNTTLA CFVAILIGLC
401 LTLLLAVFK KALPALPISI TFGLIFYFST DNLVRPFMDT LASHQLYI

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## (57) Abstract

The present invention discloses nucleic acid molecules encoding AD4 gene products, expression vectors and host cells suitable for expressing such gene products. Also disclosed are methods for treating, preventing, and diagnosing Alzheimer's Disease.

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 96/11386

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 C07K14/47 A01K67/00 C12N15/12 //C12Q1/68

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 6 C07K

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)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 96 34099 A (HSC RESEARCH AND DEVELOPMENT LP) 31 October 1996 see the whole document ---	1-46
X,P	SCIENCE, vol. 269, 18 August 1995, LANCASTER, PA US, pages 973-977, XP000616667 LEVY-LAHAD E. ET AL.: "Candidate gene for the chromosome 1 familial Alzheimer's disease locus" see the whole document --- -/--	1-6, 14-19, 32-37,46

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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- "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.
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Date of the actual completion of the international search

17 February 1997

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International Application No

PCT/US 96/11386

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	<p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 92, no. 12, December 1995, pages 12180-12184, XP000604928 LI J ET AL: "IDENTIFICATION AND EXPRESSION ANALYSIS OF A POTENTIAL FAMILIAL ALZHEIMER DISEASE GENE ON CHROMOSOME 1 RELATED TO AD3" see abstract see page 12180, column 2, paragraph 5 see page 12183, column 2, paragraph 4 see figures 3,4</p> <p style="text-align: center;">---</p>	<p>1-3,6, 14-19, 32-37,46</p>
X,P	<p>NATURE, vol. 376, 31 August 1995, LONDON GB, pages 775-778, XP000196835 ROGAEV E.I. ET AL.: "Familial Alzheimer's disease in kindreds with missense mutations in a gene on chromosome 1 related to the Alzheimer's disease type 3 gene" see the whole document</p> <p style="text-align: center;">---</p>	<p>1-6, 32-37,46</p>
A	<p>SCIENCE, vol. 258, 23 October 1992, LANCASTER, PA US, pages 668-671, XP000616263 SCHELLEMBERG G.D. ET AL.: "Genetic linkage evidence for a familial Alzheimer's disease locus on chromosome 14." cited in the application</p> <p style="text-align: center;">-----</p>	

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 96/11386

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9634099	31-10-96	AU-A- 5394096	18-11-96
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