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(54) Title: PD-L2 MOLECULES: PD-1 LIGANDS AND USES THEREFOR

(57) Abstract: The invention provides isolated nucleic acid molecules, designated PD-L2 nucleic acid molecules, which encode novel B7-related molecules which are ligands for PD-1. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing PD-L2 nucleic acid molecules, host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a PD-L2 gene has been introduced or disrupted. The invention further provides isolated PD-L2 polypeptides, fusion proteins, antigenic peptides and anti-PD-L2 antibodies. The invention still further provides methods for promoting or inhibiting the interaction between PD-L2 and PD-1. Diagnostic and treatment methods utilizing compositions of the invention are also provided.

INTERNATIONAL SEARCH REPORT

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**A. CLASSIFICATION OF SUBJECT MATTER**  
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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)  
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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)  
EPO-Internal, WPI Data, BIOSIS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DONG H ET AL: "B7-H1, A THIRD MEMBER OF THE B7 FAMILY, CO-STIMULATES T-CELL PROLIFERATION AND INTERLEUKIN-10 SECRETION" NATURE MEDICINE, NATURE PUBLISHING, CO, US, vol. 5, no. 12, December 1999 (1999-12), pages 1635-1639, XP002942544 ISSN: 1078-8956 the whole document	1,2
P,X	WO 01 39722 A (CHEN LIEPING ;MAYO FOUNDATION (US)) 7 June 2001 (2001-06-07) claims 25-32; examples 3-5,8-12	1,2
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Further documents are listed in the continuation of box C.       Patent family members are listed in annex.

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 International Application No  
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FREEMAN G J ET AL: "The B7 homologue, PD-L is the ligand of the PD-1 immunoinhibitory receptor" FASEB JOURNAL, FED. OF AMERICAN SOC. FOR EXPERIMENTAL BIOLOGY, BETHESDA, MD, US, vol. 14, no. 6, May 2000 (2000-05), page a1170 XP002202702 ISSN: 0892-6638 the whole document ---	1,2
P,X	WO 01 14557 A (DANA FARBER CANCER INST INC ;GENETICS INST (US)) 1 March 2001 (2001-03-01) claim 27; examples 6-17 ---	1,2
P,X	FREEMAN G ET AL: "ENGAGEMENT OF THE PD-1 IMMUNOINHIBITORY RECEPTOR BY A NOVEL B7 FAMILY MEMBER LEADS TO NEGATIVE REGULATION OF LYMPHOCYTE ACTIVATION" JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP, vol. 192, no. 7, 2 October 2000 (2000-10-02), pages 1027-1034, XP000971650 ISSN: 0022-1007 the whole document ---	1,2
E	WO 02 00730 A (DANA FARBER CANCER INST INC ;GENETICS INST (US)) 3 January 2002 (2002-01-03) see whole document particularly claims 59 and 61 ---	1,2
E	WO 01 94413 A (SQUIBB BRISTOL MYERS CO) 13 December 2001 (2001-12-13) page 130 -page 132 ---	1,2
E	WO 02 08279 A (MILLENIUM PHARMACEUTICALS INC) 31 January 2002 (2002-01-31) page 60 -page 64 ---	1,2
E	WO 01 83750 A (TSENG SU YI ;GORSKI KEVIN S (US); PARDOLL DREW M (US); TSUCHIYA HA) 8 November 2001 (2001-11-08) the whole document ---	1,2
	-/--	

## INTERNATIONAL SEARCH REPORT

 International Application No  
 PCT/US 01/20858

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>           TSENG SU-YI ET AL: "B7-DC, a new dendritic cell molecule with potent costimulatory properties for T cells"            JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP,            vol. 193, no. 7,            2 April 2001 (2001-04-02), pages 839-845,            XP002193883            ISSN: 0022-1007            the whole document            ---         </p>	1,2
P,X	<p>           LATCHMAN YVETTE ET AL: "PD-L2 is a second ligand for PD-1 and inhibits T cell activation"            NATURE IMMUNOLOGY, NATURE PUBLISHING GROUP,, GB,            vol. 2, no. 3, March 2001 (2001-03), pages 261-268, XP001064842            ISSN: 1529-2908            the whole document            ---         </p>	1,2
A	<p>           AGATA Y ET AL: "EXPRESSION OF THE PD-1 ANTIGEN ON THE SURFACE OF STIMULATED MOUSE T AND B LYMPHOCYTES"            INTERNATIONAL IMMUNOLOGY, OXFORD UNIVERSITY PRESS, GB,            vol. 8, no. 5, May 1996 (1996-05), pages 765-772, XP000971773            ISSN: 0953-8178            the whole document            -----         </p>	1,2

## INTERNATIONAL SEARCH REPORT

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0139722	A	07-06-2001	AU 2053001	A 12-06-2001
			EP 1234031	A2 28-08-2002
			WO 0139722	A2 07-06-2001
WO 0114557	A	01-03-2001	AU 6800500	A 19-03-2001
			AU 7072700	A 19-03-2001
			BR 0013542	A 14-05-2002
			BR 0013581	A 02-07-2002
			EP 1210424	A1 05-06-2002
			EP 1210428	A1 05-06-2002
			NO 20020859	A 22-04-2002
			NO 20020861	A 19-04-2002
			US 2002102651	A1 01-08-2002
			WO 0114556	A1 01-03-2001
			WO 0114557	A1 01-03-2001
WO 0200730	A	03-01-2002	AU 7173101	A 08-01-2002
			AU 7309601	A 08-01-2002
			WO 0200692	A2 03-01-2002
			WO 0200730	A2 03-01-2002
			US 2002110836	A1 15-08-2002
WO 0194413	A	13-12-2001	AU 7528501	A 17-12-2001
			WO 0194413	A2 13-12-2001
			US 2002095024	A1 18-07-2002
WO 0208279	A	31-01-2002	AU 7602601	A 05-02-2002
			WO 0208279	A2 31-01-2002
			US 2002106730	A1 08-08-2002
WO 0183750	A	08-11-2001	AU 5570001	A 12-11-2001
			WO 0183750	A2 08-11-2001
			US 2002091246	A1 11-07-2002