



(12) Translation of
European patent specification

(11) NO/EP 2935329 B1

NORWAY

(19) NO
(51) Int Cl.
C07K 16/28 (2006.01)
G01N 33/574 (2006.01)
G01N 33/577 (2006.01)

Norwegian Industrial Property Office

(45)	Translation Published	2021.01.25
(80)	Date of The European Patent Office Publication of the Granted Patent	2020.09.16
(86)	European Application Nr.	13814812.7
(86)	European Filing Date	2013.12.18
(87)	The European Application's Publication Date	2015.10.28
(30)	Priority	2012.12.21, US, 201261745386 P
(84)	Designated Contracting States:	AL ; AT ; BE ; BG ; CH ; CY ; CZ ; DE ; DK ; EE ; ES ; FI ; FR ; GB ; GR ; HR ; HU ; IE ; IS ; IT ; LI ; LT ; LU ; LV ; MC ; MK ; MT ; NL ; NO ; PL ; PT ; RO ; RS ; SE ; SI ; SK ; SM ; TR
	Designated Extension States:	BA ; ME
(73)	Proprietor	Merck Sharp & Dohme Corp., 126 East Lincoln Avenue, Rahway, NJ 07065-0907, USA
(72)	Inventor	PIERCE, Robert, H., 712 Bryant Street 5, San Francisco, California 94107, USA BOURNE, Patricia, 901 S. California Avenue, Palo Alto, California 94304, USA LIANG, Linda, 901 S. California Avenue, Palo Alto, California 94304, USA BIGLER, Michael, 901 S. California Avenue, Palo Alto, California 94304, USA
(74)	Agent or Attorney	TANDBERG INNOVATION AS, Postboks 1570 Vika, 0118 OSLO, Norge

(54)	Title	ANTIBODIES THAT BIND TO HUMAN PROGRAMMED DEATH LIGAND 1 (PD-L1)
(56)	References Cited:	WO-A1-2013/173223 SHENG-JIA SHI ET AL: "B7-H1 Expression Is Associated with Poor Prognosis in Colorectal Carcinoma and Regulates the Proliferation and Invasion of HCT116 Colorectal Cancer Cells", PLOS ONE, vol. 8, no. 10, 4 October 2013 (2013-10-04), page e76012, XP055110544, DOI: 10.1371/journal.pone.0076012 THOMPSON R H ET AL: "Tumor B7-H1 is associated with poor prognosis in renal cell carcinoma patients with long-term follow-up", CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, US, vol. 66, no. 7, 1 April 2006 (2006-04-01), pages 3381-3385, XP008091321, ISSN: 0008-5472, DOI: 10.1158/0008-5472.CAN-05-4303 CHEN BENJAMIN J ET AL: "PD-L1 Expression Is Characteristic of a Subset of Aggressive B-cell Lymphomas and Virus-Associated Malignancies", CLINICAL CANCER RESEARCH, THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, US, vol. 19, no. 13, 1 July 2013 (2013-

07-01), pages 3462-3473, XP009177218, ISSN: 1078-0432 [retrieved on 2013-05-14]

DING H ET AL: "PD-L1 is expressed by human renal tubular epithelial cells and suppresses T cell cytokine synthesis", CLINICAL IMMUNOLOGY, ACADEMIC PRESS, US, vol. 115, no. 2, 1 May 2005 (2005-05-01), pages 184-191, XP004879483, ISSN: 1521-6616, DOI: 10.1016/J.CLIM.2005.01.005

HOLGER KRÖNIG ET AL: "PD-1 expression on Melan-A-reactive T cells increases during progression to metastatic disease", INTERNATIONAL JOURNAL OF CANCER, vol. 130, no. 10, 11 January 2012 (2012-01-11), pages 2327-2336, XP055110549, ISSN: 0020-7136, DOI: 10.1002/ijc.26272

J. HAMANISHI ET AL: "Programmed cell death 1 ligand1 and tumor-infiltrating CD8+ T lymphocytes are prognostic factors of human ovarian cancer", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 104, no. 9, 27 February 2007 (2007-02-27), pages 3360-3365, XP055030513, ISSN: 0027-8424, DOI: 10.1073/pnas.0611533104

JULES GADIOT ET AL: "Overall survival and PD-L1 expression in metastasized malignant melanoma", CANCER, vol. 117, no. 10, 29 November 2010 (2010-11-29), pages 2192-2201, XP055107383, ISSN: 0008-543X, DOI: 10.1002/cncr.25747 cited in the applicati on

DONG HUA: "B7-H1 expression is associated with expansion of regulatory T cells in colorectal carcinoma", WORLD JOURNAL OF GASTROENTEROLOGY, vol. 18, no. 9, 1 January 2012 (2012-01-01), page 971, XP055110548, ISSN: 1007-9327, DOI: 10.3748/wjg.v18.i9.971

LIANCAI WANG ET AL: "Clinical Significance of B7-H1 and B7-1 Expressions in Pancreatic Carcinoma", WORLD JOURNAL OF SURGERY ; OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF SURGERY/SOCIÉTÉ INTERNATIONALE DE CHIRURGIE, SPRINGER-VERLAG, NE, vol. 34, no. 5, 10 February 2010 (2010-02-10), pages 1059-1065, XP019800514, ISSN: 1432-2323

DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; 2013, BIGELOW ELAINE ET AL: "Immunohistochemical staining of B7-H1 (PD-L1) on paraffin-embedded slides of pancreatic adenocarcinoma tissue.", XP002722587, Database accession no. NLM23328703 -& Elaine Bigelow ET AL: "Immunohistochemical staining of B7-H1 (PD-L1) on paraffin-embedded slides of pancreatic adenocarcinoma tissue.", Journal of visualized experiments : JoVE, 1 March 2013 (2013-03-01), XP055111169, Retrieved from the Internet: URL:<http://www.jove.com/video/4059/immunohistochemicalstaining-b7-h1-pd-l1-on-parafin-embedded-slides> [retrieved on 2014-04-01]

WU C ET AL: "Immunohistochemical localization of programmed death-1 ligand-1 (PD-L1) in gastric carcinoma and its clinical significance", ACTA HISTOCHEMICA, ELSEVIER, AMSTERDAM, NL, vol. 108, no. 1, 10 May 2006 (2006-05-10), pages 19-24, XP027962807, ISSN: 0065-1281 [retrieved on 2006-05-10]

HONG LI ET AL: "The characteristic expression of B7-associated proteins in Langerhans cell sarcoma", ACTA HISTOCHEMICA, ELSEVIER, AMSTERDAM, NL, vol. 114, no. 7, 21 December 2011 (2011-12-21), pages 733-743, XP028399033, ISSN: 0065-1281, DOI: 10.1016/J.ACTHIS.2011.12.010 [retrieved on 2012-01-12]

Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (<http://worldwide.espacenet.com>) or via the search engine on our website here: <https://search.patentstyret.no/>

Patentkrav

1. Et isolert antistoff eller antigenbindende fragment som spesifikt binder PD-L1 hvor:

(a) den lette kjedens variable område er SEKV ID NR:13 og den tunge kjedens variable område er SEKV ID NR:20; eller

(b) den lette kjedens variable område er SEKV ID NR:25 og den tunge kjedens variable område er SEKV ID NR:32, hvor X i SEKV ID NR:32 er Q eller pE.

2. Det isolerte antistoffet eller antigenfragmentet ifølge krav 1 hvor X i SEKV ID NR:32 er Q.

3. En isolerte nukleinsyre som koder for de variable områdene av antistoffet eller det antigenbindende fragmentet ifølge krav 1, hvor X i SEKV ID NR:32 er Q.

4. Den isolerte nukleinsyren ifølge krav 3, som er en ekspresjonsvektor.

5. En vertscelle som omfatter ekspresjonsvektoren ifølge krav 4.

6. En fremgangsmåte for å analysere en vevsprøve fjernet fra et menneske for PD-L1 ekspresjon, hvor fremgangsmåten omfatter:

(a) å kontakte vevsprøven med et PD-L1 bindingsreagens under betingelser som tillater spesifikk binding av PD-L1 bindingsreagenset til humant PD-L1, hvor bindingsreagenset omfatter antistoffet eller det antigenbindende fragmentet ifølge et hvilket som helst av kravene 1 til 2,

(b) å fjerne ubundet PD-L1 bindingsreagens, og

(c) å påvise nærværet eller fraværet av bundet PD-L1 bindingsmiddel.

7. Fremgangsmåten ifølge krav 6, som videre omfatter å kvantifisere mengden av bundet bindingsreagens.

8. Et sett som omfatter det isolerte antistoffet eller det antigenbindende fragmentet derav ifølge et hvilket som helst av kravene 1 eller 2 og et sett av reagenser for å påvise et kompleks av antistoffet eller det antigenbindende fragmentet bundet til humant PD-L1.

9. Settet ifølge krav 8, hvor antistoffet eller det antigenbindende fragmentet omfatter SEKV ID NR: 13 og SEKV ID NR:20, eller omfatter SEKV ID NR:25 og SEKV ID NR:32, hvor X i SEKV ID NR:32 er Q.