



(51) International Patent Classification:

A61K 39/395 (2006.01) C07K 14/47 (2006.01)
A61P 35/00 (2006.01) C07K 16/18 (2006.01)

(21) International Application Number:

PCT/US2017/013511

(22) International Filing Date:

13 January 2017 (13.01.2017)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/278,815 14 January 2016 (14.01.2016) US

(71) Applicants: MEMORIAL SLOAN-KETTERING CAN-
CER CENTER [US/US]; 1275 York Avenue, New York,
NY 10065 (US). EUREKA THERAPEUTICS, INC.
[US/US]; 5858 Horton Street, Suite 362, Emeryville, CA
94608 (US).

(72) Inventors: SCHEINBERG, David, A.; 325 Central Park
West, New York, NY 10025 (US). DAO, Tao; 245 87th,

Apt. 14F, New York, NY 10128 (US). LIU, Cheng; 4
Commodore Drive, #D334, Emeryville, CA 94608 (US).

(74) Agents: KOLE, Lisa, B. et al.; Baker Botts LLP, 30 Rock-
efeller Plaza, New York, NY 10112-4498 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN,
KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA,
MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG,
NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS,
RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY,
TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,
ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ,
TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU,

[Continued on next page]

(54) Title: T CELL RECEPTOR-LIKE ANTIBODIES SPECIFIC FOR FOXP3-DERIVED PEPTIDES

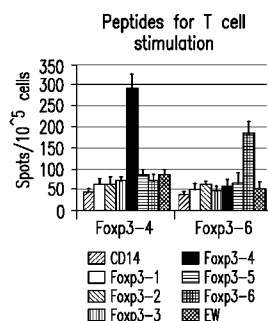


FIG. 1A

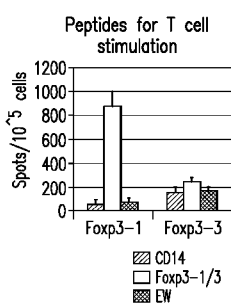


FIG. 1C

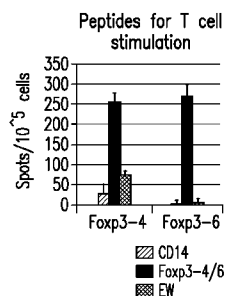


FIG. 1B

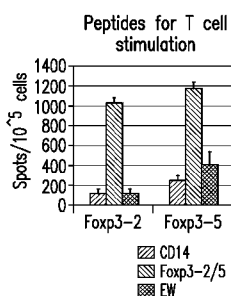


FIG. 1D

(57) Abstract: The presently disclosed subject matter provides antigen-
binding proteins (e.g., chimeric antigen receptors) and antibodies or an-
tigen-binding portions thereof that bind to a Foxp3 peptide/MHC mo-
lecle complex. Such antibodies, fusion proteins and conjugates thereof
are useful for inhibiting regulatory T cells and treating cancers.



TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(88) Date of publication of the international search report:

17 August 2017

Published:

— *with international search report (Art. 21(3))*

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 17/13511

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 39/395, A61P 35/00, C07K 14/47, C07K 16/18 (2017.01)

CPC - A61K 39/39558, C07K 14/47, C07K 16/18, A61K 39/39533, A61K 39/3955, A61K 39/395

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)

See Search History Document

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

See Search History Document

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

See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y --- A	US 2010/0143359 A1 (EBERT et al.) 10 June 2010 (10.06.2010) para [0083, [0123]; SEQ ID NO: 12	1-5, 7/(1-5) ----- 6, 7/6, 60-61 ----- 38-41
Y	US 2013/0287748 A1 (JUNE et al.) 31 October 2013 (31.10.2013) abstract; para [0005], [0006], [0008], [0009], [0053], [0081], [0110], [0111]	60-61
Y	WO 2015/070061 A1 (MEMORIAL SLOAN-KETTERING CANCER CENTER et al.) 14 May 2015 (14.05.2015) abstract; para [00151]	6, 7/6
A	US 2009/0324579 A1 (PANDEY et al.) 31 December 2009 (31.12.2009) SEQ ID NO: 3	38-41
A	US 2014/0011982 A1 (BURNHAM INSTITUTE FOR MEDICAL RESEARCH) 9 January 2014 (09.01.2014) SEQ ID NO: 127	38-41
A	JP 2006/197930 A (HIROSHIMA PREFECTURE) 3 August 2006 (03.08.2006) SEQ ID NO: 2	38-41
A	WO 2015/189638 A2 (QUEEN MARY UNIVERSITY OF LONDON) 17 December 2015 (17.12.2015) SEQ I	38-41

☒ Further documents are listed in the continuation of Box C.

☐ See patent family 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 application or patent 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

1 June 2017

Date of mailing of the international search report

17 JUL 2017

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-8300

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 17/13511

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2012/0117685 A1 (WU et al.) 10 May 2012 (10.05.2012) SEQ ID NO: 7730	38-41
A	US 2012/0005773 A1 (AASEN et al.) 5 January 2012 (05.01.2012) SEQ ID NO: 8535	38-41
A	US 2013/0333068 A1 (COFFIN) 12 December 2013 (12.12.2013) SEQ ID NO: 53542	38-41
A	US 2009/0324512 A1 (SILENCE et al.) 31 December 2009 (31.12.2009) SEQ ID NO: 21	38-41
A	US 2010/0003253 A1 (LAEREMANS et al.) 7 January 2010 (07.01.2010) SEQ ID NO: 96	38-41
A	US 2013/0136744 A1 (ABLYNX N.V.) 30 May 2013 (30.05.2013) SEQ ID NO: 21	38-41
A	A0A0M3QYJ1, UniProtKB/TrEMBL Accession No. A0A0M3QYJ1, 9 December 2015 [online]. [Retrieved on 1 June 2017]. Retrieved from the internet <URL: http://www.uniprot.org/uniprot/A0A0M3QYJ1.txt?version=1 > entire document	38-41
A	M0JRF5, UniProtKB/TrEMBL Accession No. M0JRF5, 27 May 2015 [online]. [Retrieved on 1 June 2017]. Retrieved from the internet <URL: http://www.uniprot.org/uniprot/M0JRF5.txt?version=4 > entire document	38-41
A	G0MBP3, UniProtKB/TrEMBL Accession No. G0MBP3, 9 December 2015 [online]. [Retrieved on 1 June 2017]. Retrieved from the internet <URL: http://www.uniprot.org/uniprot/G0MBP3.txt?version=12 > entire document	38-41
A	US 2003/0059427 A1 (FORCE et al.) 27 March 2003 (27.03.2003) SEQ ID NO: 16	38-41
A	US 2010/0234578 A1 (MIKAYAMA et al.) 16 September 2010 (16.09.2010) SEQ ID NO: 64	38-41
A	US 2011/0014211 A1 (AZUMA et al.) 20 January 2011 (20.01.2011) SEQ ID NO: 52	38-41
A	WO 2015/097536 A2 (JANSSEN PHARMACEUTICA NV) 2 July 2015 (02.07.2015) SEQ ID NO: 37	38-41
A	US 2009/0137002 A1 (PETRUL et al.) 28 May 2009 (28.05.2009) SEQ ID NO: 23	38-41
A	US 2013/0102031 A1 (ANAPTYSBIO, INC.) 25 April 2013 (25.04.2013) SEQ ID NO: 23	38-41
A	WO 2009/003489 A1 (NATIMMUNE AS) 8 January 2009 (08.01.2009) SEQ ID NO: 2	38-41
A	US 2012/0058906 A1 (SMIDER et al.) 8 March 2012 (08.03.2012) SEQ ID NO: 1642	38-41
A	US 2014/0030273 A1 (VERPLOEGEN et al.) 30 January 2014 (30.01.2014) SEQ ID NO: 7	38-41
A	US 2013/0323249 A1 (ZHOU et al.) 5 December 2013 (05.12.2013) SEQ ID NO: 134	38-41
A	US 2007/0072177 A1 (BAKKER et al.) 29 March 2007 (29.03.2007) SEQ ID NO: 196	38-41

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 17/13511

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 8-37, 42-57, 59, 62-83
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

-----please see extra sheet-----

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
Group I+: Claims 1-7, 38-41, limited to SEQ ID NOs: 9-14, 93-94
Group I+: Claims 1-7, 38-41, limited to SEQ ID NOs: 39-44, 103-104
Group III+: Claims 60-61, limited to SEQ ID NO: 8
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☒ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 17/13511

Continuation of: Box No. III Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I+: Claims 1-7, 38-41, drawn to an isolated antibody, or an antigen-binding portion thereof, which binds to a Foxp3 peptide bound to a human major histocompatibility complex (MHC) molecule. The antibody will be searched to the extent that the antibody cross-competes for binding, or binds to the same epitope as a reference antibody comprising:

- a heavy chain variable region CDR1 comprising an amino acid sequence set forth in SEQ ID NO: 9; a heavy chain variable region CDR2 comprising an amino acid sequence set forth in SEQ ID NO: 10; a heavy chain variable region CDR3 comprising an amino acid sequence set forth in SEQ ID NO: 11; a light chain variable region CDR1 comprising an amino acid sequence set forth in SEQ ID NO: 12; a light chain variable region CDR2 comprising an amino acid sequence set forth in SEQ ID NO: 13; and a light chain variable region CDR3 comprising an amino acid sequence set forth in SEQ ID NO: 14 (claims 38, 39)

- a heavy chain variable region comprising an amino acid sequence set forth in SEQ ID NO: 93, and a light chain variable region that comprising an amino acid sequence set forth in SEQ ID NO: 94 (claims 40, 41)

It is believed that claims 1-7, 38-41, limited to SEQ ID NOs: 9-14 and 93-94, encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass an isolated antibody that cross-competes for binding, or binds to the same epitope as a reference antibody comprising SEQ ID NOs: 9-14 and 93-94.

Additional antibodies will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected antibodies. Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched. An exemplary election would be an antibody cross-competes for binding, or binds to the same epitope as a reference antibody comprising:

- a heavy chain variable region CDR1 comprising an amino acid sequence set forth in SEQ ID NO: 15; a heavy chain variable region CDR2 comprising an amino acid sequence set forth in SEQ ID NO: 16; a heavy chain variable region CDR3 comprising an amino acid sequence set forth in SEQ ID NO: 17; a light chain variable region CDR1 comprising an amino acid sequence set forth in SEQ ID NO: 18; a light chain variable region CDR2 comprising an amino acid sequence set forth in SEQ ID NO: 19; and a light chain variable region CDR3 comprising an amino acid sequence set forth in SEQ ID NO: 20 (claims 38,39)

- a heavy chain variable region comprising an amino acid sequence set forth in SEQ ID NO: 95, and a light chain variable region that comprising an amino acid sequence set forth in SEQ ID NO: 96 (claims 40, 41)

i.e. claims 1-7, 38-41, limited to SEQ ID NOs:15-19, 95-96.

Group II: Claim 58, drawn to a method for detecting Foxp3 in a whole cell or tissue.

Group III+: Claim 60-61, drawn to a chimeric antigen receptor (CAR) specific for a Foxp3 peptide bound to a human MHC molecule.

Group II+ will be searched upon payment of additional fees. The CAR may be searched for an additional fee and election as such, for example, to the extent that the Foxp3 peptide encompasses SEQ ID NO: 8, i.e. claims 60-61 limited to SEQ ID NO: 8. Additional Foxp3 peptides will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected Foxp3 peptides. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched. Another exemplary election would be wherein the Foxp3 peptide encompasses SEQ ID NO: 2, i.e. claims 60-61 limited to SEQ ID NO: 2.

The inventions listed as Groups I+, II, and III+ do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features

Group I+ requires a composition comprising an isolated antibody, or an antigen-binding portion thereof, which binds to a Foxp3 peptide bound to a human major histocompatibility complex (MHC) molecule, not required by Groups II and III+. Further, the technical feature of each of the inventions listed as Group I+ is the specific antibody sequences recited therein. Each invention requires antibody sequences, not required by any of the other inventions.

Group II requires method steps for detecting Foxp3 in a whole cell or tissue, not required by Groups I+ and III+.

Group III+ requires a chimeric antigen receptor (CAR), not required by Groups I+ and II. Further, the technical feature of each of the inventions listed as Group III+ is the specific Foxp3 peptide sequence recited therein. Each invention requires a Foxp3 peptide sequence, not required by any of the other inventions.

-----please see next extra sheet-----

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 17/13511

Continuation of: Box No. III Observations where unity of invention is lacking

Common Technical Features

The feature shared by Groups I+, II, and III+ is a protein that binds to a Foxp3 peptide bound to a human MHC molecule.

Another feature shared by Groups I+ and II is an antibody or an antigen-binding portion thereof that binds to a Foxp3 peptide bound to a human MHC molecule.

Another feature shared by the inventions listed as Group I+ is an isolated antibody, or an antigen-binding portion thereof, which binds to the same epitope on a Foxp3 peptide bound to an MHC molecule with a reference antibody or antigen-binding portion, wherein the cross-competing antibody or antigen-binding portion thereof specifically binds to the Foxp3 peptide/MHC complex with a binding affinity (KD) of about 5×10^{-7} M or less (claims 38, 40)

Another feature shared by the inventions listed as Group I+ is an isolated antibody, or an antigen-binding portion thereof, which binds to the same epitope on a Foxp3 peptide bound to an MHC molecule with a reference antibody or antigen-binding portion thereof (claims 39, 41).

However, these shared technical features do not represent a contribution over prior art, because the shared technical features are taught by US 2010/0143359 A1 to Ebert et al. (hereinafter 'Ebert').

Ebert discloses a protein that binds to a Foxp3 peptide bound to a human MHC molecule (para [0108] The invention also involves the use of agents such as polypeptides that bind to FoxP3 polypeptides"; para [0110] "In preferred embodiments, the binding polypeptide is an antibody or antibody fragment").

Ebert discloses [claim 1] an isolated antibody, or an antigen-binding portion thereof, which binds to a Foxp3 peptide bound to a human major histocompatibility complex (MHC) molecule (para [0123] "The antibodies of the present invention can also be used to therapeutically target FoxP3 polypeptides. In one embodiment, antibodies can be used to target FoxP3 antigens expressed on the cell surface, such as FoxP3 peptides presented by MHC molecules. This can be accomplished, for example, by raising antibodies that recognize the complex of FoxP3 peptides and MHC molecules").

Ebert discloses [claims 38, 40] an isolated antibody, or an antigen-binding portion thereof, which binds to a Foxp3 peptide bound to a human major histocompatibility complex (MHC) molecule (para [0123] "antibodies that recognize the complex of FoxP3 peptides and MHC molecules"). Ebert does not specifically teach that the antibody crosscompetes for binding to a Foxp3 peptide bound to a human MHC molecule with a reference antibody, wherein the cross-competing antibody or antigen-binding portion thereof specifically binds to the Foxp3 peptide/MHC complex with a binding affinity (KD) of about 5×10^{-7} M or less. However, Ebert does teach that the antibody selectively binds to Foxp3 (para [0108] "The invention also involves the use of agents such as polypeptides that bind to FoxP3 polypeptides"; para [0110] "In preferred embodiments, the binding polypeptide is an antibody or antibody fragment, such as an Fab or F(ab)2 fragment of an antibody. Typically, the fragment includes a CDR3 region that is selective for the FoxP3 polypeptide"; para [0111] "Thus, the invention provides agents which bind to FoxP3 polypeptides encoded by FoxP3 nucleic acid molecules of the invention, and in certain embodiments preferably to unique fragments of the FoxP3 polypeptides . . . such binding partners can be used to selectively target drugs, toxins or other molecules (including detectable diagnostic molecules) to cells which express FoxP3 polypeptides"; para [0123] "antibodies that recognize the complex of FoxP3 peptides and MHC molecules"). Given that the antibody of Ebert selectively binds to Foxp3 peptide/MHC complex, one of ordinary skill in the art would have found it obvious that the antibody would compete for binding to the same epitope on Foxp3 as a reference peptide that binds with high affinity to Foxp3 peptide/MHC complex. Thus, an antibody that cross competes for binding to a Foxp3 peptide/MHC complex with a reference antibody, wherein the cross-competing antibody or antigen-binding portion thereof specifically binds to the Foxp3 peptide/MHC complex with a binding affinity (KD) of about 5×10^{-7} M or less, would have been obvious in view of Ebert.

Ebert discloses [claims 39, 41] an isolated antibody, or an antigen-binding portion thereof, which binds to a Foxp3 peptide bound to a human major histocompatibility complex (MHC) molecule (para [0123] "antibodies that recognize the complex of FoxP3 peptides and MHC molecules"). Ebert does not specifically teach that the antibody binds to the same epitope on a Foxp3 peptide bound to an MHC molecule with a reference antibody or antigen-binding portion thereof. However, Ebert does teach that the antibody selectively binds to Foxp3 peptide/MHC complex (para [0108] "The invention also involves the use of agents such as polypeptides that bind to FoxP3 polypeptides"; para [0110] "In preferred embodiments, the binding polypeptide is an antibody or antibody fragment, such as an Fab or F(ab)2 fragment of an antibody. Typically, the fragment includes a CDR3 region that is selective for the FoxP3 polypeptide"; para [0111] "Thus, the invention provides agents which bind to FoxP3 polypeptides encoded by FoxP3 nucleic acid molecules of the invention, and in certain embodiments preferably to unique fragments of the FoxP3 polypeptides . . . such binding partners can be used to selectively target drugs, toxins or other molecules (including detectable diagnostic molecules) to cells which express FoxP3 polypeptides"; para [0123] "antibodies that recognize the complex of FoxP3 peptides and MHC molecules"). Given that the antibody of Ebert selectively binds to Foxp3 peptide/MHC complex, one of ordinary skill in the art would have found it obvious that the antibody would compete for binding to the same epitope on Foxp3 as a reference peptide that binds with high affinity to Foxp3 peptide/MHC complex. Thus, an isolated antibody, or an antigen-binding portion thereof, which binds to the same epitope on a Foxp3 peptide bound to an MHC molecule with a reference antibody or antigen-binding portion would have been obvious in view of Ebert.

As the technical features were known in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the groups.

-----please see next extra sheet-----

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 17/13511

Continuation of: Box No. III Observations where unity of invention is lacking

The feature shared by the inventions listed as Group III+ is a chimeric antigen receptor (CAR) specific for a Foxp3 peptide bound to a human MHC molecule (claim 60).

However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is taught by Ebert in view of US 20130287748 A1 to June et al. (hereinafter 'June').

Ebert discloses [claim 60] an isolated antibody, or an antigen-binding portion thereof, which binds to a Foxp3 peptide bound to a human major histocompatibility complex (MHC) molecule (para [0123] "antibodies that recognize the complex of FoxP3 peptides and MHC molecules").

Ebert does not teach a chimeric antigen receptor (CAR). However, June discloses a chimeric antigen receptor (CAR) for treating cancer, wherein the CAR comprises an antigen binding domain (abstract "The present invention provides compositions and methods for treating cancer in a human. The invention includes relates to administering a genetically modified T cell to express a CAR wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain"; para [0005] "the CAR comprises an antigen binding domain"). June further teaches that the antigen binding domain can be an antibody that targets a tumor antigen (para [0008] "the antigen binding domain in the CAR is an antibody or an antigen-binding fragment thereof"; para [0009] "the antigen binding domain in the CAR binds to a tumor antigen"). Given that June teaches a CAR that comprises an antigen binding domain, wherein the antigen binding domain comprises an antibody targeting a tumor antigen, and Ebert discloses that the antibody specific for Foxp3 can be used as an antigen targeting domain that binds to a tumor antigen (para [0110] "In preferred embodiments, the binding polypeptide is an antibody or antibody fragment, . . . that is selective for the FoxP3 polypeptide"; para [0111] "the invention provides agents which bind to FoxP3 polypeptides . . . such binding partners can be used to selectively target drugs, toxins or other molecules (including detectable diagnostic molecules) to cells which express FoxP3 polypeptides"; para [0006] "the expression of FoxP3 by tumor cells may represent a novel mechanism by which cancers suppress the immune system in order to escape destruction"; para [0053] "The invention relates in part to the discovery that FoxP3 polypeptides and nucleic acid molecules that encode the FoxP3 polypeptides are expressed in cancer cells and tumors"), one of ordinary skill in the art would have found it obvious that a CAR as taught by June can comprise an antibody which binds to a Foxp3 peptide bound to a MHC, as taught by Ebert.

As the technical feature was known in the art at the time of the invention, it cannot be considered a special technical feature that would otherwise unify the groups.

Groups I+, II, and III+ therefore lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.