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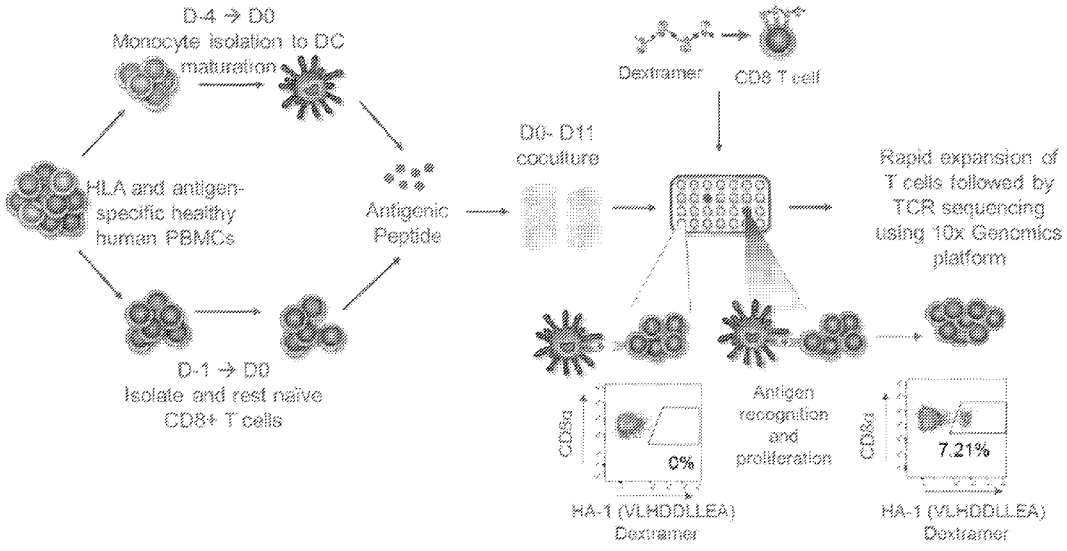
(54) Title: BINDING PROTEINS RECOGNIZING HA-1 ANTIGEN AND USES THEREOF

FIG. 1



(57) Abstract: Provided herein are binding proteins recognizing HA-1 antigen and uses thereof.

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[Continued on next page]

Published:

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

— *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))*

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 21/58382

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61P 35/00, C07K 14/705, C07K 14/71, C07K 14/725 (2022.01)

CPC - A61P 35/00, A61P 35/02, C07K 14/70503, C07K 14/7051

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 ------ A	US 2020/0231649 A1 (FRED HUTCHINSON CANCER RESEARCH CENTER) 23 July 2020 (23.07.2020) abstract; para [0063]-[0067]; [0083]-[0090]; [0100]-[0101]; [0135]; [0151]-[0152]; SEQ ID NOs: 38 and 92	1-4, 7/(1-4), 32-35 ------ 5-6, 7/(5-6), 31
A	US 2012/0027739 A1 (JAKOBSEN et al.) 02 February 2012 (02.02.2012) abstract; para [0091]-[0092]; SEQ ID NO: 13	5-6, 7/(5-6), 31
A	CHAN et al., Divergent T-cell receptor recognition modes of a HLA-I restricted extended tumour-associated peptide. Nature communications. March 2018, Vol 9, article 1026, pg: 1-3. full document	1-7, 31-35

☐ 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
"D" document cited by the applicant in the international application
"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	Date of mailing of the international search report
28 March 2022	APR 28 2022
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 Karl Rodriquez Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 21/58382

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☒ furnished subsequent to the international filing date for the purposes of international search only:

      ☒ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. ☒ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 21/58382

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.: 8-30, 36-138, 142-149
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:
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 searched, the appropriate additional search fees must be paid.

Group I+: Claims 1-7, 31-35, drawn to a T cell receptor (TCR) binding protein that is capable of binding to HA-1 immunogenic peptide-MHC complex or a nucleic acid encoding it. The TCR binding protein will be searched to the extent that the TCR alpha chain CDRs, V.alpha chain, and full TCR alpha chain have at least 80% sequence identity to the first named polypeptide sequence in instant application pg 51 Table 1, HA1-TSC-100 wild type sequence alpha sequence, SEQ ID NO: 1. It is believed that claims 1-7, 31-35 read on this first named invention and thus these claims will be searched without fee to the extent that they have at least 80% sequence identity and are encompassed by SEQ ID NO: 1. Additional TCR binding proteins comprising TCR alpha or beta chain CDRs, V.alpha or V.beta chain, and full TCR alpha or beta chain will be searched upon payment of additional fees. Applicant must specify the claims that encompass any additional elected TCR alpha or beta chain CDRs, V.alpha or V.beta chain, and full TCR alpha or beta chain. Applicants must further indicate, if applicable, the claims which read on 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/examined. An exemplary election would be: Table 1 HA1-1-12 CDTM sequence Alpha chain SEQ ID NO: 5 (claims 1-7, 31-35) --continued on 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.:

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.:
1-7, 31-35, limited to at least 80% identity to SEQ ID NO: 1 (HA1-TSC-100 alpha)

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.

--continued from Box III Unity of invention is lacking--

Group II: Claims 139-141, drawn to an expression vector comprising a promoter operably linked to a nucleic acid sequence encoding CD8.alpha and/or CD8.beta.

The inventions listed as Groups I+ and II 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:

Technical Features:

Group I+ has the special technical feature of a binding protein capable of binding to HA-1 immunogenic peptide-MHC complex, not required by Group II.

Group I+ inventions share the special technical feature of a TCR alpha chain CDR sequences, V.alpha domain and full length TCR alpha chain polypeptide sequences or nucleic acid sequences encoding them, not required by Group II.

Group I+ inventions share the special technical feature of a TCR beta chain CDR sequences, V.beta domain and full length TCR beta chain polypeptide sequences or nucleic acid sequences encoding them, not required by Group II.

Group II has the special technical feature of an expression vector comprising a promoter operably linked to a nucleic acid sequence encoding CD8.alpha and/or CD8.beta, not required by Group I+.

No technical features are shared between the polypeptide sequences of Group I+ and, accordingly, this group lacks unity a priori.

Additionally, even if Groups I+ inventions and Group II were considered to share the technical features of:

1. Group I+ inventions share the technical feature of a binding protein comprising a TCR alpha chain CDR sequences, V.alpha domain and full length TCR alpha chain polypeptide sequences or nucleic acid sequences encoding them and/or a TCR beta chain CDR sequences, V.beta domain and full length TCR beta chain polypeptide sequences or nucleic acid sequences encoding them, wherein the binding protein is capable of binding to HA-1 immunogenic peptide-MHC complex.

2. Group I+ and II share the technical feature of a nucleic acid encoding a cell surface protein.

However, said shared technical features do not represent a contribution over the prior art and are disclosed by US 10,538,574 B2 to Fred Hutchinson Cancer Research Center (hereinafter "Hutch") [published 21 January 2020].

As to shared technical feature #1, Hutch discloses a binding protein comprising a TCR alpha chain CDR sequences, V.alpha domain and full length TCR alpha chain polypeptide sequences (claim 1; "An engineered immune cell, comprising a heterologous polynucleotide encoding a binding protein that includes: (a) a TCR alpha-chain variable (V.alpha) domain comprising a CDR3 amino acid sequence of SEQ ID NO: 88, a CDR2 amino acid sequence of SEQ ID NO: 136, and a CDR1 amino acid sequence of SEQ ID NO: 135, and; (b) a TCR beta-chain variable (V.beta) domain comprising a CDR3 amino acid sequence of SEQ ID NO: 14, a CDR2 amino acid sequence of SEQ ID NO: 134, and a CDR1 amino acid sequence of SEQ ID NO: 133, wherein the encoded binding protein is capable of specifically binding to a peptide containing an HA-1H antigen and does not bind to a peptide that does not contain an HA-1H antigen").

As to common technical feature #2, Hutch discloses a nucleic acid encoding a cell surface protein (claim 1; "An engineered immune cell, comprising a heterologous polynucleotide encoding a binding protein").

As the shared technical features were known in the art at the time of the invention, they cannot be considered shared special technical features that would otherwise unify the groups. The inventions lack unity with one another.

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

Item 4 (cont.): Claims 8-30, 36-138, 142-149 are dependent claims and are not drafted according to the second and third sentences of PCT Rule 6.4(a).