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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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(54) Title: COMPOSITIONS OF EMBEDDED EPITOPE RANDOM PEPTIDES (EERP) FOR TREATMENT OF IMMUNE-MEDIATED CONDITIONS, AND METHODS OF USE

1 7 12 50

Ac-XXXXXXAYKAAAXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-amide

Embedded Epitope

Fig. 1

(57) **Abstract:** Embedded Epitope Random Peptides (EERP) for the treatment of autoimmune diseases are provided. Each EERP is a polypeptide consisting of a random sequence of three or more amino acids in a specific molar ratio, within which is embedded an epitope composed of a specific amino acid sequence. Also provided is a method of treating an autoimmune disease or condition using the EERP.

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INTERNATIONAL SEARCH REPORT

International application No.
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A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 31/785; A61K 38/00; A61K 38/02; A61K 38/03; A61K 38/07; A61K 38/16 (2022.01)
CPC - A61K 38/02; A61K 38/2026; A61K 38/2066; A61K 38/215 (2022.05)

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	US 2012/0276049 A1 (PRESIDENT AND FELLOWS OF HARVARD COLLEGE) 01 November 2012 (01.11.2012) entire document	1, 2
A	US 2015/0030560 A1 (PRESIDENT AND FELLOWS OF HARVARD COLLEGE et al) 29 January 2015 (29.01.2015) entire document	1, 2
A	US 2007/0264229 A1 (STROMINGER) 15 November 2007 (15.11.2007) entire document	1, 2
A	US 9,028,835 B2 (STROMINGER et al) 12 May 2015 (12.05.2015) entire document	1, 2
A	US 2020/0246394 A1 (SYNLOGIC OPERATING COMPANY INC.) 06 August 2020 (06.08.2020) entire document	1, 2

☐ 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
29 April 2022	JUN 03 2022
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Harry Kim Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
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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.: 10-22
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:

See extra sheet(s).

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, 2

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.
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Continued from 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 need to be paid.

Group I+: claims 1-9 are drawn to amino acid copolymers.

The first invention of Group I+ is restricted to an amino acid copolymer having the sequence (X)0-195(Z)5-20(X)0-195, where X is selected to be zero (absent), and Z is selected to be AYKAA. It is believed that claims 1 and 2 read on this first named invention and thus these claims will be searched without fee to the extent that they read on AYKAA.

Applicant is invited to elect additional amino acid copolymers to be searched in a specific combination by paying additional fee for each set of election. An exemplary election would be an amino acid copolymer having the sequence (X)0-195(Z)5-20(X)0-195, where each instance of X is selected to be 1, further selected to be tyrosine(Y), and Z is selected to be AYKAA. Additional amino acid copolymers will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. 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.

The inventions listed in Groups I+ 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:

The Groups I+ formulas do not share a significant structural element responsible for interacting with MHC class II proteins and T-cell receptors, requiring the selection of alternative amino acid copolymers where "an amino acid copolymer having the sequence (X)0-195 (Z)5-20(X)0-195 wherein X is one of tyrosine(Y), phenylalanine(F), alanine(A), and lysine(K); and Z consists of a peptide epitope that interacts with a major histocompatibility complex (MHC) class II protein and a T cell receptor."

Additionally, even if Groups I+ were considered to share the technical features of an amino acid copolymer having the sequence (X) 0-195(Z)5-20(X)0-195 wherein X is one of tyrosine(Y), phenylalanine(F), alanine(A), and lysine(K); and Z consists of a peptide epitope that interacts with a major histocompatibility complex (MHC) class II protein and a T cell receptor. However, these shared technical features do not represent a contribution over the prior art.

Specifically, US 2007/0264229 A1 to Strominger discloses an amino acid copolymer having the sequence (X)0-195(Z)5-20(X)0-195 wherein X is one of tyrosine(Y), phenylalanine(F), alanine(A), and lysine(K) (a composition having a peptide comprising an amino acid sequence selected from the group consisting of: YEAYK, Para. [0005]; a pharmaceutical composition having at least one peptide from the group of peptides having amino acid sequences: EKAKYEAYKAAAAAA (SEQ ID NO: 1), Para. [0012]); and Z consists of a peptide epitope that interacts with a major histocompatibility complex (MHC) class II protein and a T cell receptor (an amino acid sequence capable of inhibiting an immune response in a subject, Para. [0014]; also featured is an isolated peptide composition that binds to a MHC class II protein HLA-DR2 and stimulates proliferation of Th2 secreting T cells, Para. [0015]; binding to HLA-DR2, and for inhibition of proliferation of two T cell hybridomas that carry the TCR derived from two different MS patients, Para. [0042]).

The inventions listed in Groups I+ therefore lack unity under Rule 13 because they do not share a same or corresponding special technical features.