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(54) Title: INTERLEUKIN-15 FUSION PROTEIN AND METHODS OF USE

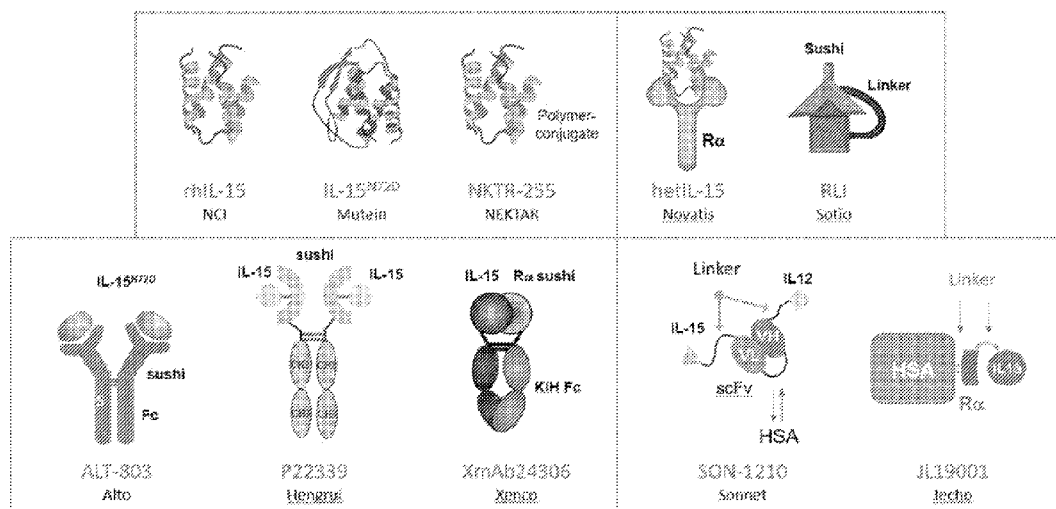


FIG. 1

(57) Abstract: The disclosure provides IL-15 fusion proteins as well as compositions comprising them. Specifically, the fusion protein comprising at least one of an IL-15Ra sequence and/or an IL-15 sequence fused to an albumin protein. The disclosure further provides methods of treating and/or preventing immunodeficiency as well as methods for cancer immunotherapy in a subject, wherein the method includes administering a fusion protein as described herein.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 24/31723

A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. A61K 45/00, A61P 35/00, A61K 39/00, A61K 38/38, C07K 17/00, C07H 21/04 (2024.01)
ADD. C12P 21/04 (2024.01)

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ADD. C12N 5/16, C07K 2319/00, C07K 2317/24, C07K 2319/31

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	WO 2021/030688 A1 (IGM BIOSCIENCES, INC.) 18 February 2021 (18.02.2021), para [0006], [0016], [0101], [0134], [0140], [0155], [0201], and pg 79, SEQ ID NO: 27	1-3 ---- 4 ---- 10
Y	CHARLES et al., Prevention of Human Rhinovirus Infection by Multivalent Fab Molecules Directed against ICAM-1. Antimicrob Agents Chemother. 2003, Vol. 47(5), p. 1503-1508. Abstract; pg 1503, col 1, lower para and col 2, top para; and pg 1506, col 1, para 3	4
A	WO 2021/142476 A1 (DRAGONFLY THERAPEUTICS, INC.) 15 July 2021 (15.07.2021), para [0004], [0008], [0071], [0072], [0197], and pg 52, SEQ ID NO: 68	1-4, 10
A	US 2019/0365861 A1 (XENCOR, INC.) 05 December 2019 (05.12.2019), Abstract, para [0009]-[0017], [0087], [0433], [0703], and [0980]	1-4, 10
A	US 2012/0177595 A1 (WONG, et al.) 12 July 2012 (12.07.2012), Abstract, and para [0115]	1-4, 10
A	US 2014/0113370 A1 (CAMPHAUSEN et al.) 24 April 2014 (24.04.2014), Abstract, and pg 31, Table 13	1-4, 10
A	CHEN et al., A targeted IL-15 fusion protein with potent anti-tumor activity. Cancer Biol Ther. 2015, Vol. 16(9), P. 1415-1421. Entire documentation especially Abstract; pg 1415, col 1, and col 1, middle para and last para; and pg 1416, Fig 1	1-4, 10



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

"I" 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

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Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 24/31723

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HSU et al., Preclinical Evaluation of Recombinant Human IL15 Protein Fused with Albumin Binding Domain on Anti-PD-L1 Immunotherapy Efficiency and Anti-Tumor Immunity in Colon Cancer and Melanoma. Cancers (Basel). 2021, Vol. 13(8): 1789. PDF File: pg 1-25. Entire documentation especially Abstract	1-4, 10

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 24/31723

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.
 - b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13ter.1(a)),
☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.
2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 24/31723

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.: 5-9, 11-25
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.

Groups I+, claims 1-4, 10, directed to a fusion protein comprising at least one of an IL-15Ra sequence and/or an IL-15 sequence fused to an albumin protein (claims 1-4), and a fusion protein comprising a sequence specified (claim 10). The fusion protein comprising a sequence specified will be searched to the extent that the fusion protein encompasses SEQ ID NO: 1 [Specification, Table 1, pg 32-34, wherein each of SEQ ID NOs: 1-6 and 8 represents a different IL-15 and/or IL-15Ra albumin fusion protein), based on the guidance set forth in section 10.54-10.55 of the PCT International Search and Preliminary Examination Guidelines. It is believed that claims 1-4, 10(in part) encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass a fusion protein comprising at least one of an IL-15Ra sequence and/or an IL-15 sequence fused to an albumin protein, and a fusion protein comprising a sequence of SEQ ID NO: 1. *****Continued in the 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.: 1-4, 10(in part), limited to SEQ ID NO: 1

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.

Continuation of:
Box No III (unity of invention is lacking)

(Continuation of Groups I+) Additional fusion protein comprising SEQ ID NO specified will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected fusion protein comprising SEQ ID NO specified. 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 a fusion protein comprising at least one of an IL-15Ra sequence and/or an IL-15 sequence fused to an albumin protein, and a fusion protein comprising a sequence of SEQ ID NO: 2. [claims (1-4), 10(in part)].

The inventions listed as 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:

Special Technical Feature

Among Groups I+, each SEQ ID NO represents a structurally different protein sequence.

Common Technical Features

The inventions of Groups I+ share the technical features of a fusion protein comprising at least one of an IL-15Ra sequence and/or an IL-15 sequence fused to an albumin protein, and wherein the fusion protein comprising a sequence specified.

However, these shared technical features do not represent a contribution over prior art as being anticipated by WO 2021/030688 A1 to IGM BIOSCIENCES, INC. (hereinafter 'IGM') as follows:

IGM discloses a fusion protein (para [0006] - 'Sushi domain/IL-15 fusion proteins') comprising --at least one of an IL-15Ra sequence and/or an IL-15 sequence fused to an albumin protein (para [0134] - 'a modified J-chain comprising IL-15 and/or the IL-15 receptor-a sushi domain fused thereto'; para [0201] - 'non-J-chain constructs in which IL-15 and the IL-15 receptor a sushi domain are fused to human serum albumin'). IGM further discloses wherein the fusion protein comprising a sequence specified (para [0134] - 'a modified J-chain comprising IL-15 and/or the IL-15 receptor-a sushi domain fused thereto'; para [0201] - 'IL-15 and the IL-15 receptor a sushi domain are fused to human serum albumin ..."HRI," SEQ ID NO: 27'; pg 76, Table 10: Sequence Presented in the Disclosure; pg 79, HSA fusion HRI, SEQ ID NO: 27; para [0140] - 'human serum albumin (HSA)').

Without a shared special technical feature, the inventions lack unity with one another.

Groups I+ therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Note: Claims 5-9, 11-25 have been held unsearchable because they are not drafted in accordance with the second and third sentences of Rule 6.4(a).