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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))

(54) Title: SIALIDASE FUSION MOLECULES AND RELATED USES

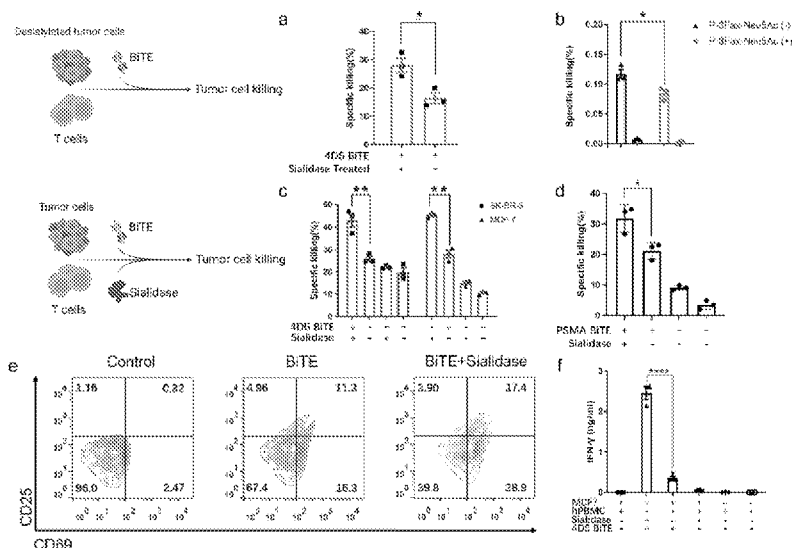


FIG. 1

(57) **Abstract:** The invention provides fusion molecules that contain a sialidase and a bispecific molecule that engages an immune cell (e.g., T cell or NK cell) and a target cell underlying a disease. Related polynucleotides, vectors and host cells are also described herein. The invention further provides therapeutic applications of the sialidase fusions in treating cancer.

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29 February 2024 (29.02.2024)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 23/66586

A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. C12N 9/24, A61K 39/395, C07K 16/28, A61P 35/00 (2023.01)
ADD.

CPC - INV. C12N 9/2402, A61K 39/0011, C07K 16/2827, A61P 35/00

ADD. C12Y 302/01018, C07K 2317/31, C07K 2317/622, C07K 2319/01

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 2020/252208 A2 (MYELOID THERAPEUTICS, INC.) 17 December 2020 (17.12.2020) para [0017], [0027], [0052], [0094], [00136], [00137], [00159], [00167], [00230], [00374], [00381], claims 1, 13, 38.	1-4, 9, 10, 23-24, 27-29 ----- 11, 12, 19 ----- 20
Y	WO 2022/020473 A2 (THE SCRIPPS RESEARCH INSTITUTE) 27 January 2022 (27.01.2022) para [0057], claims 1, 4, 5, 6.	11, 12
Y --- A	WO 2019/091384 A1 (YAFEI SHANGHAI BIOLOG MEDICINE SCIENCE & TECHNOLOGY CO, LTD.) 16 May 2019 (16.05.2019) SEQ ID NO: 70	19 ---- 20

☐ 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

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 23/66586

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 23/66586

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.:
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:
Go to Extra Sheet for continuation

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, 9-12, 19, 20, 23, 24, 27-29, limited to BiTE, BiTE engages CD3, human sialidase, C-terminal linkage, SEQ ID NO: 6

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 23/66586

continuation of Box 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 searched, the appropriate additional search fees must be paid.

Group I+: Claims 1-24, 27-29, drawn to a fusion polypeptide comprising a bispecific molecule and a sialidase.

The fusion polypeptide will be searched to the extent that the bispecific molecule is the first named, a bispecific T cell engager (BiTE)(claim 3), specifically engages T cell specific molecule CD3 (claim 4), the sialidase is human sialidase (claim 11), the sialidase is fused by the first named linkage, at the C-terminus of the bispecific molecule, and the bispecific molecule is the first named polypeptide, at least 95% identical to SEQ ID NO: 6. This first named invention has been selected based on the guidance set forth in section 10.54 of the PCT International Search and Preliminary Examination Guidelines. It is believed that claims 1-4, 9-12, 19, 20, 23, 24, 27-29 read on this first named invention and thus these claims will be searched without fee to the extent that they encompass BiTE that specifically engages CD3, human sialidase, linkage is the C-terminus of the bispecific molecule and the bispecific molecule is at least 95% identical to SEQ ID NO: 6

Additional fusion polypeptides will be searched upon payment of additional fees. Applicant must specify the claims that encompass any additional cell type engagers, source of sialidase, fusion linkages, and specific bispecific molecule SEQ ID NOs. 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: bispecific innate cell engager, macrophage cell, specifically CD16A, human sialidase, sialidase fused at N-terminus of the bispecific molecule, bispecific molecule has at least 95% identity to SEQ ID NO: 32 (claims 1-8, 10-16, 38-43, 45).

Group II: Claims 25, 26, drawn to a method of treating a disease.

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:

Special Technical Features:

Group I+ has the special technical feature of a fusion polypeptide comprising a bispecific molecule and a sialidase, not required by Group II.

Group II has the special technical feature of administering a pharmaceutical composition, not required by Group I+.

Among the inventions listed as Groups I+ are the different cell type engagers, sialidases, and fusion linkages, recited therein. Each invention requires a specific cell type engager, sialidase and fusion linkage, not required by any other inventions.

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

Common Technical Features:

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

Group I+ inventions share claim 1.

Group II claim 25 depends from Group I+ claim 1, so claim 1 is shared by both Group I+ and II.

However, said common technical features do not represent a contribution over the prior art, and are disclosed by WO 2020/252208 A2 to Myeloid Therapeutics, Inc. (hereinafter "MTI").

As to claim 1, MTI discloses a fusion polypeptide comprising (a) a bispecific molecule and (b) a sialidase or enzymatic fragment thereof, wherein the bispecific molecule comprises two antibody moieties or antigen-binding fragments that respectively bind to an immune cell and an antigen associated with a disease (claim 1; "A composition comprising a first therapeutic agent, wherein the therapeutic agent comprises: (a) a first binding domain, wherein the first binding domain is a first antibody or functional fragment thereof that specifically interacts with an antigen on a target cell, and (b) a second binding domain, wherein the second binding domain is a second antibody or functional fragment thereof that specifically interacts with a myeloid cell; wherein, (i) the first therapeutic agent is coupled to a first component, wherein the first component is an additional therapeutic agent or a third binding domain"; claim 38; "The composition of claim 1, wherein ... the additional therapeutic agent comprises ... a sialidase").

As the common technical feature was known in the art at the time of the invention, it cannot be considered a common special technical feature 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.