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[Continued on next page]

(54) Title: ANTIGEN-BINDING FUSION PROTEINS WITH MODIFIED HSP70 DOMAINS

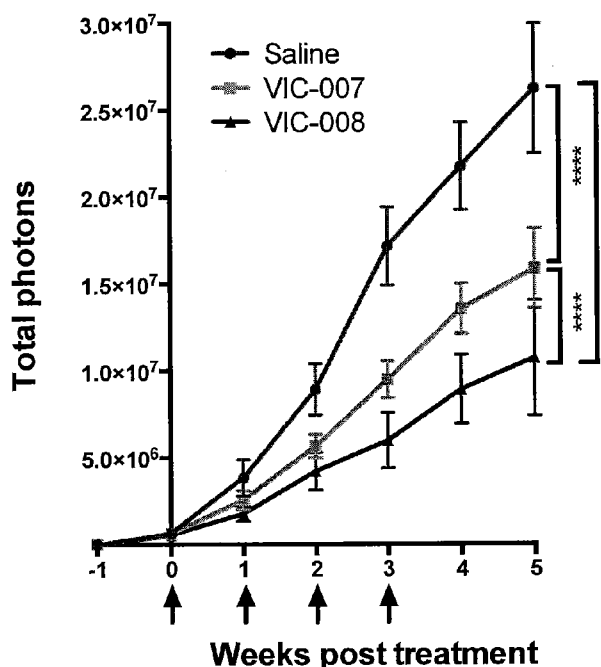


FIG. 2B

(57) Abstract: The invention relates to fusion proteins comprising an antigen binding domain fused with a modified heat shock 70 protein. The invention further relates to methods of using the fusion proteins to induce an immune response to antigens and to treat diseases associated with antigens.



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- 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/US17/21911

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 39/04, 39/12, 39/395; C12N 1/21, 15/09, 15/63, 15/70; C07K 16/28, 14/35 (2017.01)
 CPC - C12Q 1/70; G01N 33/53; A61K 39/04, 39/12, 39/395, 38/164; C12N 15/09, 15/63, 15/70; C07K 16/28, 14/35, 16/1289; C12P 21/02

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	US 2009/0068184 A1 (GELFAND, JA) 12 March 2009; paragraphs [0013], [0060], [0049], [0127], [0129], [0131]	1-2, 3/1-2, 18 ----- 20
Y	US 7,932,055 B2 (SPEE, PJL et al.) 26 April 2011; column 5, lines 39-41	20
A	US 2014/0301993 A1 (THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA) 09 October 2014; paragraphs [0011], [0016]	4/3/1-2
A	US 8,435,494 B2 (GELFAND, JA) 07 May 2013; paragraphs [0011], [0016]	4/3/1-2
A	US 2008/0085539 A1 (SCHOLLER, N et al.) 10 April 2008; paragraphs [0031], [0113]	4/3/1-2

☐ 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

"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/US17/21911

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.: 5-17, 22-24, 29-57
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 Supplemental Page-***-

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, 3/1-2, 4/3/1-2, 18, 20; SEQ ID NO: 1 (minimal HSP70 sequence) and SEQ ID NO: 3 (fusion protein sequence)

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
Information on patent family members

International application No.

PCT/US17/21911

-----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 must be paid.

Groups I+, Claims 1-4, 18-21, 25-27, SEQ ID NO: 1 and SEQ ID NO: 3 are directed toward a fusion protein comprising an antigen binding domain fused in frame to a fragment of Mycobacterium tuberculosis heat shock protein 70 (HSP70), wherein the HSP70 fragment comprises a minimal HSP70 sequence.

The fusion protein will be searched to the extent it encompasses SEQ ID NO: 1 (first exemplary minimal HSP70 sequence), or fragments thereof, and a fusion protein encompassing SEQ ID NO: 3 (first exemplary fusion protein). Applicant is invited to elect additional HSP70 sequence(s), with specified SEQ ID NO: for each, and/or fusion protein(s), with specified SEQ ID NO: for each, and/or additional domain(s), with specified SEQ ID NO: for each, to be searched. Additional HSP70 and/or fusion protein and/or additional domain sequence(s) will be searched upon the payment of additional fees. It is believed that claims 1-4, 18 and 20 (in-part) encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass SEQ ID NO: 1 (minimal HSP70 sequence) and SEQ ID NO: 3 (fusion protein sequence). Applicants must specify the claims that encompass any additionally elected HSP70 and/or fusion protein and/or additional domain sequence(s). 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/examined. An exemplary election would be an additional domain encompassing SEQ ID NO: 16 (first exemplary elected additional domain).

Group II, Claim 28 is directed toward a fusion protein comprising an antigen binding domain fused in frame to a chimeric heat shock protein 70, wherein the chimeric HSP70 comprises a backbone of a human HSP70 amino acid sequence and a substitution with residues 395 to 541 of M. tuberculosis HSP70.

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: the special technical features of Groups I+ include SEQ ID NO: 3, not present in Group II; the special technical features of Group II include SEQ ID NO: 29, not present in any of Groups I+.

No technical features are shared between the HSP70, fusion protein, and/or additional domain sequences of Groups I+ and, accordingly, these groups lack unity a priori.

Groups I+ and II share the technical features including: a fusion protein comprising an antigen binding domain fused in frame to a fragment of Mycobacterium tuberculosis heat shock protein 70 (HSP70) and SEQ ID NO: 1. Groups I+ share the technical features including: a fusion protein comprising an antigen binding domain fused in frame to a fragment of Mycobacterium tuberculosis heat shock protein 70 (HSP70), wherein the HSP70 fragment comprises a minimal HSP70 sequence of at least 100 amino acids and comprising no more than amino acids 1-495 of SEQ ID NO: 1.

However, these shared technical features are previously disclosed by US 2009/0155269 A1 (GELFAND).

Gelfand discloses a fusion protein comprising an antigen binding domain (a fusion protein comprising an antibody (antigen binding domain); abstract) fused in frame to a fragment of Mycobacterium tuberculosis heat shock protein 70 (HSP70) (fused in frame to a fragment of Mycobacterium tuberculosis heat shock protein 70 (HSP70); abstract, paragraph [0130]); SEQ ID NO: 1 (SEQ ID NO: 30 (SEQ ID NO: 1); Figure 20A, paragraph [0130], SEQ ID NO: 30, wherein SEQ ID NO: 30 is 100% identical to Applicants' SEQ ID NO: 1), and wherein the HSP70 fragment comprises a minimal HSP70 sequence of at least 100 amino acids and comprising no more than amino acids 1-495 of SEQ ID NO: 1 (wherein the HSP70 fragment comprises residues 692-819 of SEQ ID NO: 15 (wherein the HSP70 fragment comprises a minimal HSP70 sequence of at least 100 amino acids and comprising no more than amino acids 1-495 of SEQ ID NO: 1); Figure 2, SEQ ID NO: 15, wherein residues 692-819 of SEQ ID NO: 15 correspond to residues 368-485 of Applicants' SEQ ID NO: 1).

Since none of the special technical features of the Groups I+ and II inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Gelfand reference, unity of invention is lacking.