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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
19 July 2012

(54) Title: SURFACE, ANCHORED FC-BAIT ANTIBODY DISPLAY SYSTEM

(57) Abstract: The present invention provides, in part, an antibody display system that simultaneously uses a secretion and a display mode. A bait complexed with a monovalent antibody fragment can be expressed on the surface of the host cell wherein the fragment may be assayed for antigen binding while full antibody is simultaneously secreted from the host cell. Methods of using the system for identifying antibodies that bind specifically to an antigen of interest are also provided. Polypeptides, polynucleotides and host cells useful for making the antibody display system are also provided along with methods of use thereof.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/62286

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C40B 40/02, C40B 30/04 (2012.01)
USPC - 506/14
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)
IPC(8): C40B 40/02, C40B 30/04 (2012.01)
USPC: 506/14

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 506/18, 506/9, 435/7.2

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST(USPT,PGPB,EPAB,JPAB); USPTO Patent Full-Text and Image Database (US, AppFT) Google Scholar, Google Patents
Search Terms Used: antibody display, Pichia, SED-1, monovalent, sugars, glycans, Fc, fused immunoglobulin

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 2010/0009866 A1 (Prinz et al.) 14 January 2010 (14.01.2010) esp: abstract, paras [0019], [0020], [0021], [0044], [0080], [0102], [0103], [0169], [0190], [0192], [0099], [0052], [0083], [0029], [0106], [0120], [0016], [0044], [0141], [0085]-[0087], [0131], [0058], [0132], [0136], Fig. 1	1, 3/(1), 6-8, 16-18, 21-24 --- 2, 3/(2)
Y	US 2007/0105199 A1 (Yan et al.) 10 may 2007 (10.05.2007) esp: paras [0010], [0013].	2, 3/(2)
X, P	US 2010/0331192 A1 (Zha et al.) 30 December 2010 (30.12.2010) entire document.	1-3, 6-8, 16-18, 21-24
A	EP1743938 A1 Adams et al. 17 January 2007 (17.01.2007) entire document.	1-3, 6-8, 16-18, 21-24
A	US 2010/0075326 A1 (Jin et al.) 25 March 2010 esp: abstract, paras [0029], [0007], [0041], [0065], [0073], [0057], [0066], [0036], [0044], [0068].	1-3

☐ Further documents are listed in the continuation of Box C. ☐

* 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	Date of mailing of the international search report
11 May 2012 (11.05.2012)	21 MAY 2012
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. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/62286

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.: 4-5, 9-15, 19-20
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 examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-3, drawn to an antibody display system

Group II: Claims 6-8, drawn to an isolated bait polypeptide

Group III: Claims 16-18 and 24, drawn to methods for evaluating the binding of an antibody or antigen-binding fragment thereof to an antigen.

Group IV: Claims 21-23, drawn to a method for making an antibody or antigen-binding fragment thereof.

---please see continuation 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.:

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 Observations where unity of invention is lacking

The inventions listed as Groups I-IV 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 feature of the inventions listed as Groups I-IV is the generic antibody display system set forth in claim 1. This special technical feature fails to provide a contribution over the prior art, as evidenced by US 2010/0075326 A1 to Jin et al. (published 25 March 2010; hereinafter 'Jin'). Jin discloses (a) an isolated host cell (abstract; para [0029] - "The present invention provides methods and related vectors and host cells for quantitative analysis of protein interactions in eukaryotic expression system"; para [0007]); (b) a bait comprising a protein fused to a surface anchor polypeptide (para [0044] - "one protein ("bait") as a fusion to a yeast cell wall protein"); and (c) one or more polynucleotides encoding an immunoglobulin light chain variable region and (d) one or more polynucleotides encoding an immunoglobulin heavy chain variable region (para [0041] - "heavy and light chains of an antibody that retains a single active antigen-binding site"; para [0065], [0073]). Jin does not specifically teach the bait comprising a heavy Fc immunoglobulin domain, but does teach the use of bait comprising a protein fused to a surface anchor polypeptide as above. Jin also teaches the utility of a heavy Fc immunoglobulin domain in detection of specific protein/protein interactions (para [0057], [0066]) and, specifically, the antigen as the anchored"bait" and the soluble antibody as the "prey" (para [0036], [0044]). It would have been readily obvious to one of ordinary skill in the art that the"bait" and"prey" as taught by Jin could have been readily reversed resulting in a display of antibody fragments rather than antigens in an antibody display system without undue experimentation as an alternate methodology for screening protein/protein interactions as the cloning and expression of various immunoglobulin domains and domain fragments was well known and widely practiced in the art. In the absence of a contribution over the prior art, the shared technical feature is not a shared special technical feature.

Further, the special technical feature of the inventions listed as Group III are the method steps for evaluating the binding of an antibody or antigen-binding fragment thereof to an antigen. This special technical feature is not shared by the inventions of Groups I-II and IV. The special technical feature of the inventions listed as Group IV are the method steps for making an antibody or antigen-binding fragment thereof. This special technical feature is not shared by the inventions of Groups I-III.

Unity of invention exists only when the same or corresponding technical feature is shared by the claimed inventions. Without a shared special technical feature, the inventions of Groups I-IV lack unity with one another.