Abstract:

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Common Representative: MERCK SHARP & DOHME CORP.; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).

Title: Fc-containing polypeptides having increased binding to human DC-SIGN

FIG. 2

Abstract: The present invention is directed to methods and compositions for the production of Fc-containing polypeptides which are useful as human or animal therapeutic agents, and which comprise increased anti-inflammatory properties and improved CD209 (DC-SIGN) binding.
A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 39/395, A61P 1/00 (2015.01)
CPC - C07K 16/00, C07K 2317/52

According to International Patent Classification (IPC) or to both national classification and IPC

B. MINIMUM DOCUMENTATION SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61K 39/395, A61P 1/00 (2015.01)
CPC - C07K 16/00, C07K 2317/52

CPC E - A61K 39/395, A61P 1/00 (2015.01) C07K 16/00, C07K 2317/52

CPC - C07K 16/00, C07K 2317/52

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>1, 3, (6-7)/(1,3), 13-16, 18-21</td>
</tr>
<tr>
<td>A</td>
<td>US 2007/01 11281 - A1 (SONDERMANN et al.) 17 May 2007 (17.05.2007) abstract; para [0016]; [0029]; [0037]-[0041]; [0147]; [01 16]; Table 2.</td>
<td>1, 3, (6-7)/(1,3), 13-16, 18-21</td>
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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

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

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

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: 21 April 2015 (21.04.2015)

Date of mailing of the international search report: 22 May 2015

Authorized officer: Lee W. Young

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774
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.: 8-12, 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:
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.

-continued on first 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, 3-7, 13-16, 18-21

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:

Group I+, claims 1-7 and 13-21, directed to an Fc-containing polypeptide variant, a method for producing an Fc-containing polypeptide variant, a method of increasing the anti-inflammatory properties of an Fc-containing polypeptide, and a method of treating a subject with a Fc-containing peptide variant. The composition and methods listed above will be searched to the extent that the Fc-containing polypeptide mutations encompasses the first set of claimed mutations Q295R/V302A/S344P/K414R (corresponding to SEQ ID NO: 11). It is believed that claims 1, 3-7, 13-16, 18-21 encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass Fc-containing polypeptide mutations Q295R/V302A/S344P/K414R. Additional Fc-containing polypeptide mutation(s)/group(s) of mutations will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected Fc-containing polypeptide mutation(s)/group(s) of mutations. 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 Fc-containing polypeptide mutations M252V/V303A/N315S (corresponding to SEQ ID NO: 12), (claims 1, 3, 6 and 13-16, 18-21).

The inventions listed as Groups I+ do not relate to a single special technical feature 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

The inventions of Groups I+ each include the special technical feature of a unique mutation or set of mutations in an Fc-containing polypeptide. Each amino acid substitution or set of mutations is considered a distinct technical feature, because the changes in the structure-activity relationship induced by said amino acid substitution cannot readily be ascertained among these amino acid substitutions.

Shared technical features

The inventions of Group I+ share the common features of an Fc-containing polypeptide variant, a method for producing an Fc-containing polypeptide variant, a method of increasing the anti-inflammatory properties of an Fc-containing polypeptide, and a method of treating a subject with a Fc-containing peptide variant. However, these shared technical features do not represent a contribution over prior art, because the shared technical features are made obvious by reference US 2010/0189714 A1 to Ravetch et al., (hereinafter Ravetch), in view of the article entitled "Optimization of Fc-mediated effector functions of monoclonal antibodies." (Strohl) (Current opinion in biotechnology (2009) 20: 685-691).

Ravetch teaches a method for producing an Fc-containing polypeptide in a host cell (abstract, para [0043]) comprising:

a) providing a host cell comprising a nucleic acid encoding an Fc-containing polypeptide comprising one or more of mutations in the Fc region (para [0041]-[0043], [0060], claims 15 and 19), wherein the numbering is according to the EU index as in Kabat (para [0020]), culturing the host cell under conditions which cause expression of the Fc-containing polypeptide (para [0041], [0059]-[0060]), and isolating the Fc-containing polypeptide from the host cell (para [0059], claim 19).

Ravetch teaches method of treating a subject in need thereof comprising: administering to the subject a therapeutically effective amount of an Fc-containing polypeptide comprising one or more of mutations in the Fc region (claims 1, 30, para [0029]).

Ravetch teaches a method of increasing the anti-inflammatory properties of an Fc-containing polypeptide (abstract, para [0011]), comprising introducing one or more of mutations in the Fc region of the Fc-containing polypeptide (para [0029], [0041]), yet does not specifically teach the polypeptide comprises enhanced binding to human DC-SIGN when compared to a parent Fc containing polypeptide.

Strohl teaches a method of producing modified Fc-containing polypeptides with mutations that increased sialylation, wherein the polypeptide comprises enhanced binding to human DC-SIGN when compared to a parent Fc containing polypeptide (p. 688, col 2, para 2 'Sialylated mouse IgG also bind human DC-SIGN, the human counterpart of mouse SIGN-R1, in vitro'). Since Ravetch teaches the modified Fc-containing polypeptides are modified to have increased sialylation (para [0011]), one of ordinary skill in the art would have readily appreciated that the enhanced anti-inflammatory properties shown by these polypeptides is at least in part attributed to enhanced binding to human DC-SIGN, since Strohl teaches this as a mechanism for increased anti-inflammatory response of modified Fc-containing polypeptides (p. 688, col 2, para 2).

As the technical features were known in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the groups.

NOTE: Claims 8-12 and 22 are held unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).