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    G01N 33/53 (2006.01)  C12N 15/12 (2006.01)
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(71) Applicant (for all designated States except US): THE BRIGHAM AND WOMEN'S HOSPITAL INC. [US/US]; 75 Francis Street, Boston, Massachusetts 02115 (US).

(72) Inventors; and


(54) Title: METHODS FOR IDENTIFICATION AND USES OF ANTI-INFLAMMATORY RECEPTORS FOR EICOSAPENTAENOIC ACID ANALOGS

(57) Abstract: The present invention is directed to methods for the identification and uses of a receptors that interact with anti-inflammatory compounds derived from eicosapentaenoic acid (EPA). The receptors are of the G-protein coupled receptor (GPCR) family, and are useful to screen candidate substances for anti-inflammatory activity, especially substances that are analogs of EPA. Such analogs are termed "resolvins"; and are typically di- and tri-hydroxy EPA analogs. One analog herein denoted Resolvin E1 was identified in humans and prepared by total synthesis. In nanomolar range Resolvin E1 reduces dermal inflammation, peritonitis, dendritic cells (DCs) migration and IL-12 production. Also described herein is a receptor denoted Res E1 that interacts with Resolvin E1 to attenuate cytokine induced activation of inflammatory pathways mediated by transcription factor (NF)-kB. Treatment of DCs with small-interfering RNA specific for Resol E1 eliminated the ligand's ability to regulate IL-12. Assays of anti-inflammatory activity based on these discoveries are also described.
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC: G01N 33/53(2006.01),33/567(2006.01);C12N 15/12(2006.01)

USPC: 435/7.1, 7.2, 7.21; 536/23.1, 23.5

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)

U.S.: 435/7.1, 7.2, 7.21; 536/23.1, 23.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Continuation Sheet

**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>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SERHAN et al. Resolvins: A Family of Bioactive Products of Omega-3 Fatty Acid Transformation Circuits Initiated by Aspirin Treatment that Counter Proinflammation Signals. 21 October 2002, Vol. 196, No. 8, pages 1025-1037.</td>
<td>1-44</td>
</tr>
</tbody>
</table>

☐ 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 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

02 August 2006 (02.08.2006)

Date of mailing of the international search report

21 SEP 2006

Name and mailing address of the ISA/US

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Commissioner for Patents

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Form PCT/ISA/210 (second sheet) (April 2005)
Continuation of B. FIELDS SEARCHED Item 3:
CAS ONLINE, MEDLINE, CAPLUS, USPATFULL
search terms: anti-inflammatory, assay, method, Reso E receptor, resolvin, resolvin receptor, NF-kB activation
# INTERNATIONAL SEARCH REPORT

**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.: 25,35,38 and 39  
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 25,35,38 and 39  
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:  
The specific SEQ ID NOS are not recited in the claims.

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:

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 any 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.

Form PCT/ISA/210 (continuation of first sheet(2)) (April 2005)