(54) Title: DISEASE RELATED CYSTEINE MODIFICATIONS AND USES THEREOF

(57) Abstract: The present invention discloses a role for s-nitrosoglutathione in the loss of epithelial barrier integrity. The present invention is further directed to examining the therapeutic value s-nitrosoglutathione and/or a chemical entity that modifies cysteine thiol groups in regulation of intestinal mucosal integrity, function, inflammation, and pain by establishing animal models. This use of s-nitrosoglutathione and/or a chemical entity that modifies cysteine thiol groups provides a novel strategy for therapeutic intervention of pathologies associated with inflammatory barrier disorder such as inflammatory bowel disease, functional bowel disease, and infectious diarrheal disease.
A. CLASSIFICATION OF SUBJECT MATTER

A61K 38/16(2006.01)i, A61P 29/00(2006.01)i, A61P 1/00(2006.01)i

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 A61K, A61P

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
e-KIPASS, PubMed (Keywords: nitric oxide, epithelium, blood brain barrier, tight junction protein)

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></td>
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<tr>
<td>X</td>
<td>SU, L, et al., &quot;Got guts? Need nerve!&quot;, Gastroenterology, April 2007, Vol 132, No 4, pp 1615-1618 See the whole document, especially fig 1</td>
<td>7, 8, 11</td>
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<tr>
<td>A</td>
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<tr>
<td>X</td>
<td>SAVIDGE, T, C et al., &quot;Starring roles for astroglia in barrier pathologies of gut and brain&quot;, Lab Invest, July 2007 (published online), Vol 87, pp 731-736 See pages 733, 734 and table 2</td>
<td>7, 8, 11</td>
</tr>
<tr>
<td>A</td>
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</table>

Date of the actual completion of the international search 24 JUNE 2009 (24.06.2009)

Date of mailing of the international search report 24 JUNE 2009 (24.06.2009)

Name and mailing address of the ISA/KR
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Form PCT/ISA/210 (second sheet) (July 2008)
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  \(\square\) Claims Nos. 1-6, 12-23
because they relate to subject matter not required to be searched by this Authority, namely
Claims 1-6, 12-23 pertain to methods for treatment of the human by therapy, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39 l(iv) of the Regulations under the PCT, to search.

2  \(\square\) 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  \(\square\) 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  \(\square\) All required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2  \(\square\) All searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3  \(\square\) 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  \(\square\) 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

\(\square\) The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

\(\square\) 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.

\(\square\) No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (July 2008)