Abstract: The present invention provides methods of treating or preventing disorders or conditions associated with enterostatin deficiency by administering to a subject in need thereof an effective amount of enterostatin. The present invention also provides methods of selecting a subject for therapy with enterostatin. Exemplary disorders or conditions associated with enterostatin deficiency include overweight, obesity, metabolic disorders, hypertension, lipid related disorders, and type II diabetes.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61 K 38/00 (2008.01 )
USPC - 514/9; 514/17

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)

USPC - 514/9; 514/17

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)

WEST, Google Scholar: Erlanson-Albertsson Enterostatin, Enterostatin "capillary gel electrophoresis", procolipase "capillary gel electrophoresis", Enterostatin capillary gel electrophoresis, Enterostatin intra gastrically; enterostatin kit, enterostatin intraduodenally, "enterostatin assay kit"

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>X Y Y X</td>
<td>US 5,494,694 A (ERLANSON-ALBERTSSON) 27 February 1996 (27.02.1996); claim 1; col 1, In 11-16; col 2, In 5-17, 26, 31-63; col 3, In 3-6, 61-67; col 4, In 1-7</td>
<td>1-4, 6-8, 11, 18, 19, 22, 25, 42-45, 47, 69, 70, 73, 74, 77, and 80-82</td>
</tr>
<tr>
<td>Y</td>
<td>MEI et al. Enterostatin-its ability to inhibit insulin secretion and to decrease high-fat food intake. Int J Obes Relat Metab Disord. December 1993; 17(12):701-704; Abstract</td>
<td>5 and 46</td>
</tr>
<tr>
<td>X W Y</td>
<td>BOWYER et al. Effect of a satiating meal on the concentrations of procolipase propeptide in the serum and urine of normal and morbidly obese subjects. Gut 1993, 34:1500-1525; Abstract; pg 1521, col 2, para 2; pg 1522, col 1, para 1</td>
<td>26, 54-68</td>
</tr>
<tr>
<td>Y</td>
<td>MEI et al. Role of intraduodenally administered enterostatin in rats: inhibition of food. Obesity Research 1996, 4:161-165; Abstract</td>
<td>21 and 76</td>
</tr>
<tr>
<td>Y</td>
<td>US 4,948,723 A (HERMONTAYLOR et al) 14 August 1990 (14.08.1990); Abstract, col 3, In 46-67; col 4, In 1-2; col 6, In 30-39</td>
<td>83</td>
</tr>
</tbody>
</table>

Further documents are listed in the continuation of Box C

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

K Document member of the same patent family

Date of the actual completion of the international search
31 March 2008 (31.03.2008)

Date of mailing of the international search report
24 JUN 2008

Name and mailing address of the ISA/US
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Facsimile No. 571-273-3201

Authorized officer
Lee W. Young
PCT H/Ipodesk 571-272-4300 PCT OSP- 571-272-7774

Form PCT/ISA/2 10 (second sheet) (April 2007)
<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>Y</td>
<td>Lacroix et al. Laser-induced fluorescence detection schemes for the analysis of proteins and peptides using capillary electrophoresis. Electrophoresis 2005, 26:2608-2621; Abstract, pg 2608, col 2, para 1; pg 2610, col 1, para 3; col 2 para 1; pg 2620, col 1, para 1</td>
<td>61-62</td>
</tr>
</tbody>
</table>
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. 
   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. 
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6(4a)

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 from 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 1 claims 1-8, 11-26, directed to a method of treating or preventing a disorder or condition associated with enterostatin deficiency in a subject, comprising administering enterostatin to the subject, wherein claim 7 is limited to SEQ ID NO 1

Group 2 claims 27-41, directed to a method of selecting a subject for treatment with enterostatin comprising determining the amount of enterostatin in a sample from the subject

Group 3 claims 42-70 and 73-83, directed to a method of treating or preventing a disorder or condition associated with enterostatin deficiency in a subject, comprising: a) determining the amount of enterostatin in a sample from the subject, and b) administering enterostatin to the subject, wherein claim 69 is limited to SEQ ID NO 1

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.

Claims 1-8, 11-26, 42-70 and 73-83

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 2007)
INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No. PCT/US 06/47518

Continuation of:
Box No. III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

Group 4: claims 1-7, 9, 11-26, directed to a method of treating or preventing a disorder or condition associated with enterostatin deficiency in a subject, comprising administering enterostatin to the subject, wherein claim 7 is limited to SEQ ID NO: 2.

Group 5: claims 42-69, 71 and 73-83, directed to a method of treating or preventing a disorder or condition associated with enterostatin deficiency in a subject, comprising a) determining the amount of enterostatin in a sample from the subject, and b) administering enterostatin to the subject, wherein claim 69 is limited to SEQ ID NO: 2.

Group 6: claims 1-7, 10-26, directed to a method of treating or preventing a disorder or condition associated with enterostatin deficiency in a subject, comprising administering enterostatin to the subject, wherein claim 7 is limited to SEQ ID NO: 3.

Group 7: claims 42-69 and 72-83, directed to a method of treating or preventing a disorder or condition associated with enterostatin deficiency in a subject, comprising a) determining the amount of enterostatin in a sample from the subject, and b) administering enterostatin to the subject, wherein claim 69 is limited to SEQ ID NO: 3.

The inventions listed as Groups 1-7 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 technical features for the following reasons:

As to Groups 1-3, the special technical feature of Group 2 is determining the amount of enterostatin in a sample from the subject, which is not present in Group 3 that have a special technical feature of administering enterostatin to the subject;

the special technical feature of Group 1 is determining the amount of enterostatin in a sample from the subject;

the special technical feature of Group 3 is a) determining the amount of enterostatin in a sample from the subject and b) administering enterostatin to the subject, which is not present in Groups 1 and 3.

Finally, determining the amount of enterostatin in a sample from the subject is not an improvement over the article entitled "Plasma Enterostatin: Identification and Release in Rats in Response to a Meal" by MEI et al. (OBESITY RESEARCH July 2002, 10(7): 688-694) that teaches the enzyme-linked immunosorbent assay (ELISA) method for determining a level of enterostatin in blood (pg 689, col 2).

Thus, unity of invention is lacking between Groups 1-3.

As to Groups 4 and 6, under PCT Rule 13.2, unity of invention exists only when there is a shared same or corresponding special technical feature making a contribution over the prior art. The common technical feature of the listed groups is a polypeptide with enterostatin activity of SEQ ID N9:1, SEQ ID N9:2, or SEQ ID NO: 3. However, this is not an improvement over the direct submission AAL40733 to GenBank by ZUBERI et al. (01-FEB-2005, Retrieved from the Internet on 11.01.2007<http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?db=protein&id=17530175>) that teaches cofactor for pancreatic lipase encoding the pentapeptide enterostatin and comprising SEQ ID N9:1. Thus, the shared technical feature cannot function as a novel (special) technical feature to maintain unity of invention between Groups 4 and 6.

As to Groups 5 and 7, unity of invention between them lacking for reasons set forth for Groups 1, 4, and 6.

As to Groups 4 and 5, unity of invention between them lacking for reasons set forth for Groups 1 and 3.

As to Groups 6 and 7, unity of invention between them lacking for reasons set forth for Groups 1 and 3.

Therefore, unity of invention between Groups 1-7 is lacking, because they do not share a same or corresponding special technical feature.

Form PCT/ISA/210 (patent family annex) (April 2007)