METHODS OF IDENTIFYING PUTATIVE GENE PRODUCTS BY INTERSPECIES SEQUENCE COMPARISON AND BIOMOLECULAR SEQUENCES UNCOVERED THEREBY

A method of identifying alternatively spliced exons is provided. The method comprising, scoring each of a plurality of exon sequences derived from genes of a species according to at least one sequence parameter, wherein exon sequences of the plurality of exon sequences scoring above a predetermined threshold represent alternatively spliced exons, thereby identifying the alternatively spliced exons.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
   IPC: G01N 33/48(2006.01);C12Q 1/08(2006.01)
   USPC: 702/19;435/6
   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.:

   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)
   EAST; MEDLINE

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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</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
19 August 2008 (19.08.2008)

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

Date of mailing of the international search report
10 SEP 2008

Authorized officer
Marjorie Moran
Telephone No. (571) 308 1123
<table>
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<tr>
<th>Box No. II</th>
<th>Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)</th>
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<td>This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:</td>
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<tr>
<td>1. ☐</td>
<td>Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:</td>
</tr>
<tr>
<td>2. ☐</td>
<td>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:</td>
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<td>3. ☐</td>
<td>Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).</td>
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<th>Box No. III</th>
<th>Observations where unity of invention is lacking (Continuation of item 3 of first sheet)</th>
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<td>This International Searching Authority found multiple inventions in this international application, as follows: Please See Continuation Sheet</td>
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<tr>
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<td>1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.</td>
</tr>
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<td>2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.</td>
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<td>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.:</td>
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<tr>
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<td>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.: 1-16 and 18-35</td>
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**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.
BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

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, claim(s) 1-16 and 18-35, drawn to a method and system for identifying alternatively spliced exons.

Group II, claim(s) 17, drawn to a computer readable storage medium comprising data stored in a retrievable manner.

Group III, claim(s) 36-40, drawn to a group of isolated polynucleotides or polypeptides and the uses thereof.

The inventions listed as Groups I, II, and III 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:

Group I is drawn to a method or system for identifying alternatively spliced exons, comprising, scoring each of a plurality of exon sequences derived from genes of a species according to at least one parameter, wherein exon sequences of said plurality of exon sequences scoring above a predetermined threshold represent alternatively spliced exons. The study of Fairbrother et al. [Science, volume 297, 2002, pages 1007-1013] teaches predictive identification of exonic splicing enhancers in human genes. Specifically, Figure 2 on page 1009 of Fairbrother et al. teaches predicting alternatively spliced exons using their scores with a threshold of plus/minus 2.5 standard deviations. Consequently, the features of Group I are based on technical features that are not special technical features.

Conversely, Groups II and III are based on Special technical features of specific biological sequences that are not in Group I. Consequently, Groups II and III have special technical features that are not linked by general inventive concept to the invention of Group I and therefore lack unity.

If applicant decides to pay for Group III, applicant must further elect to pay for additional sequences (i.e. in addition to the first sequence) from the group of 469 sequences in Group III. Each sequence is a separate inventive entity not linked by general inventive concept to other sequences because each is a physically unique special technical feature.