Silencing TNF α targets, in particular, is useful for treating patients having or at risk of developing macular edema.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION & SUBJECT MATTER
INV. C12N15/11 A61K31/713
ADD. A61P27/02

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)
C12N A61K

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 wherever practical, search terms used)
EPO-Internal, Sequence Search, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<tr>
<th>Category</th>
<th>Citation of document with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No</th>
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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 document but published on or after the international filing date

'L' document which may throw doubts on pateny 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

'A' member of the same patent family

Date of the actual completion of the international search

18 February 2009

Date of mailing of the international search report

10/07/2009

Name and mailing address of the ISA/Authorized officer

European Patent Office, P B 5818 Patentliaa x 2 NL - 2280 HV Rijswijk Tel (+31-70) 340-2040, Fax (+31-70) 340-3016

Andres, Serge
<table>
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<td>A</td>
<td>CAMPOCHIARO P A: &quot;Potential applications for RNAi to probe pathogenesis and develop new treatments for ocular disorders&quot; GENE THERAPY, vol. 13, no. 6, 29 September 2005 (2005-09-29), pages 559-562, XP002387655 ISSN: 0969-7128 cited in the application</td>
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Continuation of Box II. 2

Claims Nos.: -

Present claim 13 associates SEQ IDs 155-201 with TNFR1 whereas the description, and especially Table 1, relates said sequences to TACE-I. In view of the positions given in e.g. claim 14 for TACE-I and which correspond to those in Table 1, it was assumed that the error lies within the wording of the claims. Hence, claim 13 has been read as concerning interfering RNAs directed to TACE-I.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.2), should the problems which led to the Article 17(2)PCT declaration be overcome.
### BOX NO. II  OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSERARCHABLE (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:
      
      **see FURTHER INFORMATION sheet PCT/ISA/210**

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:

**see additional 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 an 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.:

   **Invention 1: Cl aims 1-11 and 15-18 (all partial ly)**

**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.
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

**Invention 1.**: claims 1-11 and 15-18 (all partially)

Use of an interfering RNA directed to a region of the TNFR1 characterised by SEQ ID 59 for treating macular edema.

**Inventions 2. to 26.**: claims 1-11 and 15-18 (all partially)

As for subject 1., but concerning respectively interfering RNAs directed to regions characterised in Table 2 by nucleotides 444-479 (SEQ IDs 60-64, 96, 108-113), 531-556 (SEQ IDs 65, 116, 117), 576-612 (SEQ IDs 66, 67, 118-124), 651-678 (SEQ IDs 68-72, 125, 126), 838-843 (SEQ IDs 73, 135), 959-974 (SEQ IDs 74-77, 139-143), 1000-1026 (SEQ IDs 78, 99, 144-146), 1053-1058 (SEQ IDs 79-81, 97, 147), 1315-1324 (SEQ IDs 82, 98, 149), 1357-1360 (SEQ IDs 83, 150), 1383-1393 (SEQ IDs 84, 151), 1671 (SEQ ID 85), 2044-2048 (SEQ IDs 86-90), 2089-2098 (SEQ IDs 91-95), 328 (SEQ ID 100), 387-406 (SEQ IDs 101-105), 421-423 (SEQ IDs 106, 107), 513-517 (SEQ IDs 114, 115), 785-824 (SEQ IDs 127-134), 877-884 (SEQ IDs 136, 137), 929 (SEQ ID 138), 1161 (SEQ ID 148), 1420 (SEQ ID 152), 1471 (SEQ ID 153) and 1573 (SEQ ID 154) of SEQ ID 2.

**Invention 27.**: claims 1-11, 15-18 (all partially) and claims 12-14

Use of an interfering RNA directed to TACE-I for treating macular edema.
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