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*With international search report.*

(88) Date of publication of the international search report:
7 October 1999 (07.10.99)

(54) Title: HEPARAN SULFATE D–GLUCOSAMINYL 3–*O*–SULFOTRANSFERASES, AN USES THEREFOR


(57) Abstract

Disclosed are novel isolated nucleic acids and substancially pure protein preparations for naturally occurring and synthetic or chimeric heparan sulfate D–glucosaminyl 3–O–sulfo–transferases (3–OSTs). Also disclosed are uses for these genes and proteins, including uses for the modification and sequencing of glycosaminoglycans.

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# INTERNATIONAL SEARCH REPORT

Inter ɔnal Application No
PCT/US 98/22597

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/54 C12N9/10 C07K16/40 G01N33/68 A01K67/027

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 6 C12N

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 practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| Y | LIU J ET AL: "Purification of heparan sulfate D-glucosaminyl 3-O-sulfotransferase." J BIOL CHEM, OCT 25 1996, 271 (43) P27072-82, XP002094357 UNITED STATES cited in the application see the whole document<br>---<br>-/-- | 1-6, 8-21, 24-40, 52,53,55 |

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 17 June 1999 | 30. 06. 99 |

| Name and mailing address of the ISA | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+31-70) 340-3016 | Gurdjian, D |

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication,where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | EMEST19 DATABASE<br>Accession number AA041885<br>05-SEP-1996 (Rel. 49, Created)<br>glycosaminoglycan N-acetylglucosaminyl<br>N-deacetylase<br>Marra M. et al.<br>XP002094362 | 7 |
| Y | see the whole document | 1-6,<br>8-21,<br>26-40,<br>52,53,55 |
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| | --- | |
| X | EMEST18 DATABASE<br>Accession number AA407647<br>04-MAY-1997 (Rel. 51, Created)<br>Ko M.S.H. et al.<br>XP002094363<br>see the whole document | 7 |
| | --- | |
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| | --- | |
| A | ERIKSSON I ET AL: "cDNA cloning and sequencing of mouse mastocytoma glucosaminyl<br>N-deacetylase/N-sulfotransferase, an enzyme involved in the biosynthesis of heparin."<br>J BIOL CHEM, APR 8 1994, 269 (14) P10438-43, XP002094359<br>UNITED STATES<br>cited in the application<br>see abstract; figure 3 | 13-21,<br>26-28,<br>33-36 |
| | --- | |
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# INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 98/22597

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication,where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| A | SHWORAK NW ET AL: "Cell-free synthesis of anticoagulant heparan sulfate reveals a limiting converting activity that modifies an excess precursor pool." J BIOL CHEM, OCT 25 1996, 271 (43) P27063-71, XP002094360 UNITED STATES cited in the application see the whole document | 13-21, 26-28, 33-36 |
| A | WO 93 25659 A (UNIV MASSACHUSETTS MEDICAL) 23 December 1993 see abstract; claims 1-28 | 13-21, 26-28, 33-36 |
| Y | GB 2 295 012 A (CANCER RES CAMPAIGN TECH) 15 May 1996 see page 12, line 8 - page 14, line 2; claims 1-20 | 52,53,55 |
| X | EMBL DATABASE Accession number F07258 15-FEB-1995 Auffray C. et al. XP002106186 | 7 |
| A | see the whole document | 22,23 |
| X | EMBL DATABASE Accession number W89350 Marra M. et al. 07-JUL-1996 similar to glycosaminoglycan N-acetylglucosaminyl N-deacetylase XP002106187 | 7 |
| Y | see the whole document | 1-6, 8-13,24, 25, 28-40, 52,53,55 |
| X | EMBL DATABASE Accession number N71828 Hillier et al. 20-03-96 XP002106188 | 7 |
| A | see the whole document | 24,25 |

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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

# INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 98/22597

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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|---|---|---|
| X | EMBL DATABASE<br>Accession number T75445<br>Hillier et al.<br>25-03-95<br>similar to glycosaminoglycan<br>N-acetylglucosaminyl N-deacetylase<br>XP002106189 | 7 |
| Y | see the whole document<br>---<br>EMBL DATABASE<br>Accession number F13088<br>05-MAR-1995<br>Genexpress<br>XP002106190<br>see the whole document<br>--- | 1-6,<br>8-13,<br>28-40,<br>52,53,55<br><br>60 |
| P,X | SHWORAK NW ET AL: "Molecular cloning and expression of mouse and human cDNAs encoding heparan sulfate D-glucosaminyl 3-O-sulfotransferase."<br>J BIOL CHEM, OCT 31 1997, 272 (44)<br>P28008-19, XP002094361<br>UNITED STATES<br>see the whole document<br>----- | 1-21,<br>25-28 |

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# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 98/22597

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 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 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 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 fee, this Authority did not invite payment of any additional fee.

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.:

1-60

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.

☒ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

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

1. Claims: 14,20,21,26,27 and 1-13,15-19,28-40,44, 52-59 (partly)

   3-ost1 protein ,corresponding nucleic acid ,host cell , 3-o-sulfating saccharide method , non-human animal model , antibodies and cell line, method of identifying compounds , method of determining sequence information .

2. Claims: 22,23 and 1-13,15-19, 28-40,44,52-59 (partly)

   3-ost2 protein , corresponding nucleic acid,host cell , 3-o-sulfating saccharide method , non-human animal model , antibodies and cell line, method of identifying compounds , method of determining sequence information .

3. Claims: 24,25 and claims 1-13,15-19, 28-40,44, 52-59 (partly)

   3-ost3 proteins ,corresponding nucleic acid, host cell , 3-o-sulfating saccharide method , non-human animal model , antibodies and cell line, method of identifying compounds , method of determining sequence information .

4. Claims: 60 and 1-13,15-19, 28-40,44,52-59 (partly)

   3-ost4 protein , corresponding nucleic acid, host cell , 3-o-sulfating saccharide method , non-human animal model , antibodies and cell line, method of identifying compounds , the regulatory sequence ,method of determining sequence information .

5. Claims: 1-13,15-19, 28-40,44,52-59 (partly)

   ce3-ost protein , corresponding nucleic acid ,host cell , 3-o-sulfating saccharide method , non-human animal model , antibodies and cell line, method of identifying compounds , method of determining sequence information .

6. Claims: 1,8-12 ,29-32 (partly)

   Nucleic acid encoding heparan sulfate D-glucosaminyl 3-O-sulfotransferase, corresponnding transformed host cell and animal model with 3-ost ,as far as not covered in inventions 1-5

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

7. Claims: 33-36 (partly)

methods of producing 3-OST antibodies, antibody preparation and corresponding cell line , as far as not covered in inventions 1-5

8. Claims: 60 and 37-40 (partly )

Methods for identifying modulators of heparan sulfate D-glucosaminyl 3-O-sulfotransferase using 3-ost regulatory regions,corresponding host cell and nucleic acid with regulatory sequences , as far as not covered in inventions 1-5

9. Claims: 41-43,45-51 and 44 (partly)

method of determining partial saccharide sequence information , as far as not covered in inventions 1-5

10. Claims: 19,28 (partly)

methods of 3-o-sulfating saccharides ,as far as not covered in inventions 1-5

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Interr ıal Application No
PCT/US 98/22597

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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| GB 2295012 A | 15-05-1996 | AU 696971 B | 24-09-1998 |
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