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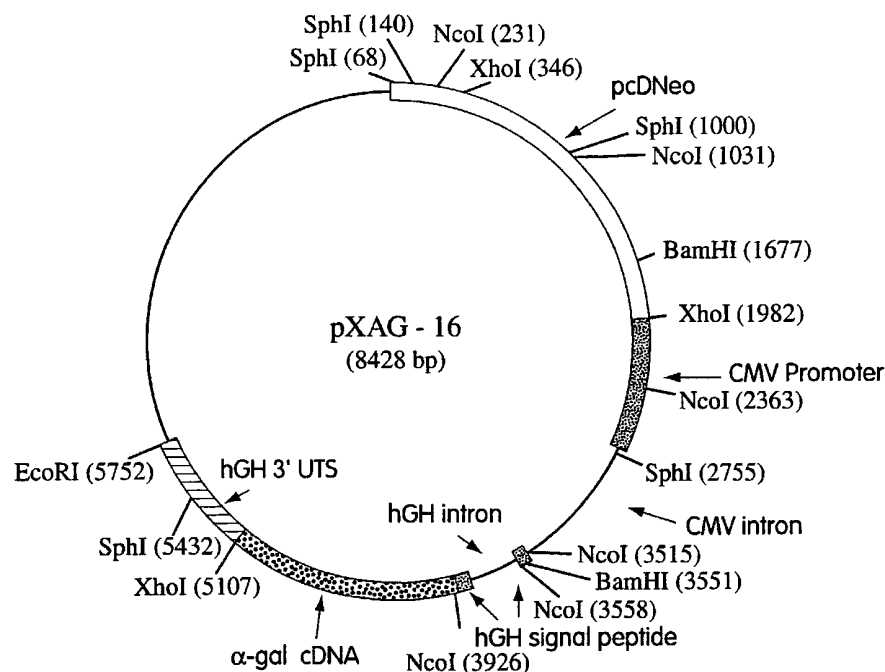
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[Continued on next page]

(54) Title: MEDICAL PREPARATIONS FOR THE TREATMENT OF ALPHA-GALACTOSIDASE A DEFICIENCY



(57) Abstract: The invention provides highly purified α -Gal A, and various methods for purifying it; α -Gal A preparations with altered charge and methods for making those preparations; α -Gal A preparations that have an extended circulating half-life in a mammalian host, and methods for making same; and methods and dosages for administering an α -Gal A preparation to a subject.



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- *With international search report.*
- *Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.*

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/06118

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/56 C12N9/40 C12N15/54 C12N15/63 C12P21/02
A61K38/46

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 7 C12N C12P 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, 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.
X A	WO 98 11206 A (TRANSKARYOTIC THERAPIES, INC.) 19 March 1998 (1998-03-19) abstract page 1, line 1 -page 2, line 32 page 5, line 19 -page 7, line 25 page 14, line 12 -page 15, line 18 page 28; table 4 page 31, line 9 - line 19 page 34, line 24 -page 37, line 22 page 44, line 6 -page 45, line 2 page 62 -page 64; claims 19,20,23,25-27,32-34 --- -/--	1,25-34 2-5,9-14

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in 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

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"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

11 September 2000

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International Application No

PC1/US 00/06118

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 94 12628 A (MOUNT SINAI SCHOOL OF MEDICINE OF THE CITY UNIVERSITY OF NEW YORK) 9 June 1994 (1994-06-09)</p> <p>abstract</p> <p>page 8, line 20 - line 30</p> <p>page 9, line 5 - line 8</p> <p>page 16, line 6 - line 13</p> <p>page 16, line 28 -page 17, line 18</p> <p>page 18, line 4 - line 13</p> <p>page 22, line 5 - line 20</p> <p>page 23, line 5 - line 21</p> <p>page 32, line 11 -page 33, line 14</p> <p>page 35, line 20 -page 36, line 5</p> <p>page 36, paragraph 5.2.5. -page 39</p> <p>page 39, paragraph 5.3.1. -page 42</p> <p>page 55, line 27 -page 56, line 20</p> <p>page 60 -page 78; example 7</p> <p>page 85 -page 90; example 9</p> <p>page 112 -page 113; claims 1-9</p> <p>---</p>	<p>1-5, 9-14, 25-34</p>
A	<p>MATSUURA, F. ET AL.: "Human alpha-galactosidase A: characterization of the N-linked oligosaccharides on the intracellular and secreted glycoforms overexpressed by Chinese hamster ovary cells"</p> <p>GLYCOBIOLOGY, vol. 8, no. 4, April 1998 (1998-04), pages 329-339, XP000925912</p> <p>cited in the application</p> <p>the whole document</p> <p>---</p>	<p>1-5, 9-14, 25-34</p>
A	<p>SBURLATI, A.R. ET AL.: "Synthesis of Bisected Glycoforms of Recombinant IFN-beta by Overexpression of beta-1,4-N-Acetylglucosaminyltransferase III in Chinese Hamster Ovary Cells"</p> <p>BIOTECHNOLOGY PROGRESS, vol. 14, no. 2, April 1998 (1998-04), pages 189-192, XP000925916</p> <p>cited in the application</p> <p>the whole document</p> <p>-----</p>	<p>1-5,9-14</p>

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/06118

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:

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.:
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.:

9-14,25-34 COMPLETELY,1-3 PARTIALLY

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

1. Claims: 9-14, 25-34 completely, 1-3 partially

A composition comprising a human alpha-Gal A preparation, purified to at least 99.5% homogeneity, comprising various alpha-Gal A glycoforms, having a specific activity of at least 3×10^6 U/mg protein and being free of lectins; a method for producing a glycosylated alpha-Gal A preparation having an increased oligosaccharid charge involving the introduction and expression of a polynucleotide encoding GlcNAc transferase III and a glycosylated alpha-Gal A preparation having an increased oligosaccharid charge produced by said method.

1.1. Claims: 25-34 completely

The use of an alpha-Gal A preparation in the manufacture of a medicament for treating Fabry disease, in particular the atypical variant of Fabry disease left ventricular hypertrophy.

2. Claims: 6-8 completely

A method for producing a purified alpha-Gal A preparation comprising various alpha-Gal A glycoforms and an alpha-Gal A preparation produced by said method.

3. Claims: 15-17 completely, 1-5 partially

A composition comprising a human alpha-Gal A preparation, purified to at least 99.5% homogeneity, comprising various alpha-Gal A glycoforms, having a specific activity of at least 3×10^6 U/mg protein and being free of lectins; a method for producing a glycosylated alpha-Gal A preparation having an increased oligosaccharid charge involving the introduction and expression of a polynucleotide encoding sialyl transferase and a glycosylated alpha-Gal A preparation having an increased oligosaccharid charge produced by said method.

4. Claims: 18, 19 completely, 1-5 partially

A composition comprising a human alpha-Gal A preparation, purified to at least 99.5% homogeneity, comprising various alpha-Gal A glycoforms, having a specific activity of at least 3×10^6 U/mg protein and being free of lectins; a method for producing a glycosylated alpha-Gal A preparation having an increased sialylation involving contacting an alpha-Gal A production cell with a culture medium having an ammonium concentration below 10 mM.

5. Claims: 20, 21 completely, 1, 2 partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A composition comprising a human alpha-Gal A preparation, purified to at least 99.5% homogeneity, comprising various alpha-Gal A glycoforms, having a specific activity of at least 3×10^6 U/mg protein and being free of lectins; a method for producing a glycosylated alpha-Gal A preparation having an increased phosphorylation involving the introduction and expression of a polynucleotide encoding a phosphoryl transferase and a glycosylated alpha-Gal A preparation having an increased phosphorylation produced by said method.

6. Claims: 22-24 completely, 1 partially

A composition comprising a human alpha-Gal A preparation, purified to at least 99.5% homogeneity, comprising various alpha-Gal A glycoforms, having a specific activity of at least 3×10^6 U/mg protein and being free of lectins; a method for producing a glycosylated alpha-Gal A preparation having a reduced number of sialic acid and terminal galactose residues on the oligosaccharide chains involving contacting alpha-Gal A with neuraminidase and contacting the desialylated alpha-Gal A with beta-galactosidase; a method for producing a glycosylated alpha-Gal A preparation having a reduced number of terminal galactose residues on the oligosaccharide chains involving contacting alpha-Gal A with beta-galactosidase and a degalactosylated alpha-Gal A preparation produced by said method.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/06118

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9811206 A	19-03-1998	AU 4424497 A	02-04-1998
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		EP 0935651 A	18-08-1999
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