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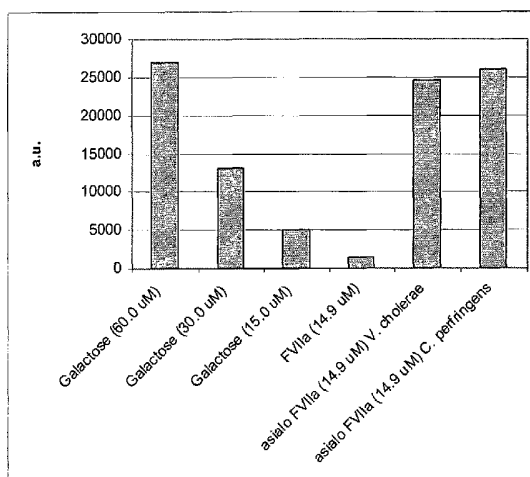
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[Continued on next page]

(54) Title: USE OF GALACTOSE OXIDASE FOR SELECTIVE CHEMICAL CONJUGATION OF PROTRACTOR
MOLECULES TO PROTEINS OF THERAPEUTIC INTEREST



Determination of exposed galactose residues after neuraminidase treatment (*Vibrio chol-
erae* and *Clostridium perfringens* on agarose), using the galactose oxidase / amplex red
assay from Molecular Probes (A-22179).

(57) Abstract: This invention relates to novel compounds, methods for selective chemical conjugation of protractor molecules and
the use thereof for diagnostic and/or therapeutic purposes.



European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

national Application No
PCT/DK2004/000530

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K38/36

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 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)

EPO-Internal, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MADNICK H M ET AL: "Effect of modification of galactose residues on the biological properties of asialo human choriogonadotropin." ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS. DEC 1981, vol. 212, no. 2, December 1981 (1981-12), pages 432-442, XP009034110 ISSN: 0003-9861 whole document; in particular abstract, p.432, right col. , p.433, right col.table I and III	1-11
X	WO 92/16555 A (ENZON INC) 1 October 1992 (1992-10-01) whole document, in particular p.9, lines 35-38, p. 18, line 36-p.19, line 5, ex.5 ----- -/-	1-16



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
- *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

15 April 2005

Date of mailing of the international search report

09.05.2005

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

National Application No
PCT/DK2004/000530

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FU QINGLAN ET AL: "Carbohydrate-directed conjugation of cobra venom factor to antibody by selective derivatization of the terminal galactose residues" BIOCONJUGATE CHEMISTRY, vol. 12, no. 2, March 2001 (2001-03), pages 271-279, XP002290190 ISSN: 1043-1802 whole document, in particular abstract, fig. 1,2, p.277, right col., last paragraph	1-11
A	EDANO TOSHIYUKI ET AL: "Importance of sialic acid in recombinant thrombomodulin in terms of pharmacokinetics and separation of desialyzed glycoprotein" BIOLOGICAL AND PHARMACEUTICAL BULLETIN, vol. 21, no. 4, April 1998 (1998-04), pages 382-385, XP009034122 ISSN: 0918-6158 whole document, in particular table I	1-11
A	RICE K G ET AL: "MODIFICATION OF TRIANTENNARY GLYCOPEPTIDE INTO PROBES FOR THE ASIALOGLYCOPROTEIN RECEPTOR OF HEPATOCYTES" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 265, no. 30, 1990, pages 18423-18428, XP002290191 ISSN: 0021-9258 the whole document	1-11
X	WO 94/28024 A (ENZON, INC) 8 December 1994 (1994-12-08) the whole document	12-16
A	US 5 714 166 A (TOMALIA ET AL) 3 February 1998 (1998-02-03) the whole document	12-16
X	US 2001/043929 A1 (ZALIPSKY SAMUEL ET AL) 22 November 2001 (2001-11-22) the whole document	12
A	US 2003/096338 A1 (PEDERSEN ANDERS HJELHOLT ET AL) 22 May 2003 (2003-05-22) the whole document	12-16
A	WO 96/36357 A (BONA, CONSTANTIN, A; LEE, Y., C; BRUMEANU, TEODOR-DORU; DEHAZYA, PHILI) 21 November 1996 (1996-11-21) the whole document	1-16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK2004/000530

Box 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 6.4(a).

Box 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 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.:

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: 1-11

A method for producing a conjugate of a glycoprotein having increased in vivo plasma half-life compared to the non-conjugated glycoprotein, the glycoprotein having at least one terminal galactose or derivative thereof, and a protractor group covalently bonded thereto, the method comprising steps (a) and (b) of claim 1.

2. claims: 12-16

A glycoprotein conjugate having increased in vivo plasma half-life compared to the non-conjugated glycoprotein, said conjugate comprising a glycoprotein having at least one terminal galactose or derivative thereof, and a protractor group covalently bonded thereto, optionally through a linking moiety.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/DK2004/000530

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INTERNATIONAL SEARCH REPORT

Information on patent family members

national Application No
PCT/DK2004/000530

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