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(54) Title: RECOMBINANT TRANSFERRIN MUTANTS

(57) Abstract: The present invention provides a recombinant protein comprising the sequence of a transferrin mutant, wherein Ser415 is mutated to an amino acid which does not allow glycosylation at Asn413 and/or wherein Thr613 is mutated to an amino acid which does not allow glycosylation as Asn61 1. It also provides polynucleotides encoding the same and methods of making and using said recombinant protein.

### INTERNATIONAL SEARCH REPORT

International application No PCT/EP2008/057508

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K38/40 A61K47/48

C:)7K14/79

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) C07K

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, WPI Data, FSTA, BIOSIS

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	WO 2006/096515 A (BIOREXIS PHARMACEUTICAL CORP [US]; SADEGHI HOMAYOUN [US]; TURNER ANDRE) 14 September 2006 (2006-09-14)	1-10,24, 25,28-45
Y	paragraphs [0015], [0012]; sequences 11, 12	11-14, 18-20, 26,27
γ	US 6 825 037 B1 (FUNK WALTER D [US] ET AL) 30 November 2004 (2004-11-30)	11-14, 18-20, 26,27
	column 15, line 64 - column 16, line 54	
	-/	

X Further documents are listed in the continuation of Box C.	X 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 filling 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 filling date but later than the priority date claimed	<ul> <li>"T" later document publishe "after the international filing date or priority date and no. in conflict with the application but cited to understand the principle or theory underlying the invention</li> <li>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the dc ument is taken alone</li> <li>"Y" document of particular relevance; the cl. imed 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.</li> <li>"&amp;" document member of the same patent family</li> </ul>
Date of the actual completion of the international search	Date of malling of the international search report
12 January 2009	19/01/2009
Name and mailing address of the ISA/  European Patent Office, P.B. 5818 Patentlaan 2  NL – 2280 HV Rijswijk  Tel. (+31–70) 340–2040,  Fax: (+31–70) 340–3016	Authorized officer Turri, Matteo

## INTERNATIONAL SEARCH REPORT

International application No
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		PCT/EP2008/057508			
C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT					
Category*	Citation of document, with Indication, where appropriate, of the relevant passages	Relevant to claim No.			
Y	BEWLEY MARIA C ET AL: "X-ray crystallography and mass spectroscopy reveal that the N-lobe of human transferrin expressed in Pichia pastoris is folded correctly but is glycosylated on serine-32" BIOCHEMISTRY, vol. 38, no. 8, 23 February 1999 (1999-02-23), pages 2535-2541, XP002508535 ISSN: 0006-2960 the whole document	26,27			
Ρ,Χ	WO 2008/012629 A (BIOREXIS PHARMACEUTICAL CORP [US]; SADEGHI HOMAYOUN [US]; PRIOR CHRIST) 31 January 2008 (2008-01-31) sequence 17	1-10,24, 25,28-45			
A	MACGILLIVRAY R T ET AL: "The complete amino acid sequence of human serum transferrin." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA APR 1982, vol. 79, no. 8, April 1982 (1982-04), pages 2504-2508, XP002497358 ISSN: 0027-8424				

International application No. PCT/EP2008/057508

## **INTERNATIONAL SEARCH REPORT**

Box No. 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:
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 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
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.
As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:  1-14, 18-20, 24-27, 28-45
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.:
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 pald within the time limit specified in the invitation.  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:

Invention 1: claims 1-4, 28-45

All subject-matter relating to a transferrin mutant wherein the Ser415 is mutated to an amino acid which does not allow glycosylation of the transferrin mutant at Asn413.

Invention 2: claims 5-9, 28-45

All subject-matter relating to a transferrin mutant wherein the Thr613 is mutated to an amino acid which does not allow glycosylation of the transferrin mutant at Asn611.

Invention 3: claims 1-10, 24, 25, 28-45

All subject-matter relating to a transferrin mutant wherein the Ser415 and Thr613 are mutated to an amino acid which does not allow glycosylation of the transferrin mutant at Asn413 and Asn611.

Invention 4: claims 1-4, 11-14, 28-45

As invention 1 wherein Asn611 is mutated to an amino acid which does not allow glycosylation of the transferrin mutant at that location.

Invention 5: claims 1-4, 15-17, 28-45

As invention 1 wherein Val612 is mutated to an amino acid which does not allow glycosylation of the transferrin mutant at that location.

Invention 6: claims 5-9, 18-20, 28-45

As invention 2 wherein Asn4131 is mutated to an amino acid which does not allow glycosylation of the transferrin mutant at that location.

Invention 7: claims 5-9, 21-23, 28-45

As invention 2 wherein Lys414 is mutated to an amino acid which does not allow glycosylation of the transferrin mutant at that location.

Inventions 7-14: claims 1-25, 26, 27, 28-45

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210						
As inventions 1-7 further comprising at least one mutation that reduces the 0-linked glycosylation.						

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2008/057508

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006096515 A	14-09-2006	CA 2599723 A1 EP 1858546 A2 JP 2008531059 T	14-09-2006 28-11-2007 14-08-2008
US 6825037 B	30-11-2004	NONE	and the same three data light label pains pring prior these years, gard
WO 2008012629 A	31-01-2008	UY 30497 A1	29-02-2008