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(54) Title: IMMUNOGENIC PRODUCTS BASED ON MUTEIN AMYLOID β (A β) AMINO ACID SEQUENCES AND USES THEREOF

(57) Abstract: The invention relates to immunogenic products based on muteinamyloid β (A β) amino acid sequences, in particular to oligomers of A β muteins, and to the use of said products in diagnosis, treatment and prevention of conditions such as amyloidoses, and for identifying agents capable of binding to said products.



WO 2016/005328 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2015/065362

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
- a. forming part of the international application as filed:
- in the form of an Annex C/ST.25 text file.
 - on paper or in the form of an image file.
- b. furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
- c. furnished subsequent to the international filing date for the purposes of international search only:
- in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
2. In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

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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:

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 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.:

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.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/065362

A. CLASSIFICATION OF SUBJECT MATTER
 INV. C07K16/18 C07K14/47 C07K7/08 A61K39/00
 ADD.
 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 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 practicable, search terms used)
 EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, SCISEARCH, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2007/062852 A2 (ABBOTT LAB [US]; ABBOTT GMBH & CO KG [DE]; BARGHORN STEFAN [DE]; EBERT) 7 June 2007 (2007-06-07) page 64 - page 66 page 71 page 73, line 7 - line 11 page 88 - page 89 examples 5-8 ----- -/--	1-99

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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</p> <p>"&" document member of the same patent family</p>
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Date of the actual completion of the international search 17 February 2016	Date of mailing of the international search report 11/04/2016
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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 Domingues, Helena
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/065362

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2010/011947 A2 (ABBOTT LAB [US]; ABBOTT GMBH & CO KG [DE]; BARGHORN STEFAN [DE]; HILLE) 28 January 2010 (2010-01-28) page 3, line 38 - line 40; figure 1 page 5, line 23 - line 25; sequence 248 page 15 page 84 - page 85 page 87 - page 88 page 119, line 21 - line 33 claims 19-20; examples 3-5 -----	1-54, 78-99
Y	WO 2012/024187 A1 (ABBOTT LAB [US]; ABBOTT GMBH & CO KG [DE]; BARGHORN STEFAN [DE]; HILLE) 23 February 2012 (2012-02-23) page 33, line 24 - line 26 example 1; sequence 45 -----	1-99
X	WO 2011/130377 A2 (ABBOTT LAB [US]; BARGHORN STEFAN [DE]; HILLEN HEINZ [DE]; STRIEBINGER) 20 October 2011 (2011-10-20) sequence 32 page 2 - page 30 examples 1-3 -----	1-51, 78-99
Y	HEINZ HILLEN ET AL: "Generation and Therapeutic Efficacy of Highly Oligomer-Specific beta-Amyloid Antibodies", JOURNAL OF NEUROSCIENCE, SOCIETY FOR NEUROSCIENCE, US, vol. 30, no. 31, 4 August 2010 (2010-08-04), pages 10369-10379, XP002650836, ISSN: 0270-6474, DOI: 10.1523/JNEUROSCI.5721-09.2010 the whole document -----	1-99

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2015/065362

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
WO 2007062852	A2	07-06-2007	AU 2006319358 A1	07-06-2007
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			WO 2011130377 A2	20-10-2011

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-99

Concerns aspects related to an immunogenic product comprising an amyloid A? amino acid sequence having 62.5% or higher identity to the amino acid sequence shown in claim 1 [Abeta(18-33); SEQ ID NO: 2] or 72% identity or higher identity to the amino acid sequence shown in claim 42 [Abeta(18-33); SEQ ID NO: 3], wherein the product is reactive with mAbs 7C6, 5F7 or 4D10 and is capable of eliciting a polyclonal serum which has no or low reactivity with PF-4.

2. claims: 100-103(partially)

Concerns aspects related to a molecule comprising an amino acid sequence identical to a portion (X-Y) of SEQ ID NO: 13 [Abeta(1-43)], with X being selected from the group consisting of the numbers 1 .. 18 and Y being selected from the group consisting of the numbers 33 .. 43; or a crosslinked derivative thereof, wherein at least 2 non-contiguous residues of the amino acid sequence are covalently linked with each other.

3-18. claims: 100-103(partially)

Each of these inventions concerns aspects related to a molecule comprising an amino acid sequence identical to a portion (X-Y) of each of the Abeta(1-43) sequences defined in claim 100, with the exception of SEQ ID NO: 13, with X being selected from the group consisting of the numbers 1 .. 18 and Y being selected from the group consisting of the numbers 33 .. 43; or a crosslinked derivative thereof, wherein at least 2 non-contiguous residues of the amino acid sequence are covalently linked with each other. Concretely, invention 3 concerns aspects related to SEQ ID NO: 14 and invention 18 concerns aspects related to SEQ ID NO: 30.
