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Previous Correction:
see Notice of 13 December 2007

(54) Title: TARGETED DELIVERY OF FGFR LIGANDS INTO THE BRAIN

(57) Abstract: The present invention relates to a compound consisting of metallothionein (MT) and a peptide sequence, wherein said peptide sequence and metallothionein are bound to each other via a non-covalent bond. A peptide sequence comprised by the compound is a biologically active short peptide sequence which comprises at most 25 amino acid residues. The peptide sequence is capable of binding to and modulating activity of a functional cell receptor, in particular fibroblast growth factor receptor (FGFR). The invention relates to pharmaceutical compositions comprising such compound or such peptide sequence and use of the compound, peptide sequence and pharmaceutical composition for treatment of conditions and diseases where modulating activity of FGFR is beneficial for treatment. In preferred embodiments the use is for treatment of conditions and diseases of the brain including conditions requiring stimulating brain cell proliferation, differentiation and/or survival, stimulating neural plasticity associated with learning and memory, modulating adhesion and motility of cells, in particular cancer cells. The compound of the invention is capable of penetrating the blood brain barrier (BBB).

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INTERNATIONAL SEARCH REPORT

International application No
PCT/DK2007/000152

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K14/825

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, BIOSIS, Sequence Search, EMBASE, MEDLINE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 03/105910 A (UNIV TASMANIA [AU]; WEST ADRIAN KEITH [AU]; CHUAH MENG INN [AU]; VICKE) 24 December 2003 (2003-12-24) cited in the application abstract; claims page 2, line 20 - page 3, line 3 page 3, line 31 - line 35 page 5, line 3 - line 6 page 10, line 16 - page 11, line 1 -----	
A	WO 03/016351 A (ENKAM PHARMACEUTICALS AS [DK]; KISELYOV VLADISLAV V [DK]; SKLADCHIKOVA) 27 February 2003 (2003-02-27) sequences 34, 37, 82, 89, 97, 99, 107, 109, 129, 136, 143, 146 the whole document ----- -/--	

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

☒ 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 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.
- *Z* document member of the same patent family

Date of the actual completion of the international search

30 November 2007

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Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

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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.
A	WO 2005/123759 A (ENKAM PHARMACEUTICALS AS [DK]; BOCK ELISABETH [DK]; BEREZIN VLADIMIR []) 29 December 2005 (2005-12-29) cited in the application sequences 2,4 the whole document -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK2007/000152

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:

Although claims 45-48 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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 allsearchable 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.:

1-25, 28 completely and claims 27, 30-48 partially

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.

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

1. claims: 1-25, 28 completely and claims 27, 30-48 partially

a compound consisting of metallothionein (MT), or a fragment thereof, and a peptide sequence comprising at most 25 contiguous amino acid residues, wherein the MT, or the fragment thereof, and the peptide sequence are bound to each other via a non-covalent bond and/or via sulfhydryl moieties of the cysteine present in the amino acid sequences of the peptide sequence and MT or the fragment thereof. The use of said compound as a medicament and for the preparation of a medicament for treatment of a disease conditions associated with activity of FGFR or FGFR ligand, method of treatment of a conditions or disease associated with activity of FGFR or a FGFR ligand.

2. claims: 26, 29 completely and 27, 30-48 partially

a peptide sequence as identified in SEQ ID Nos: 4, 8, 10, 16, 17, 26, 33, 35, 39 or 41 use of a peptide as a medicament and for the preparation of a medicament for treatment of a disease conditions associated with activity of FGFR or FGFR ligand, method of treatment of a conditions or disease associated with activity of FGFR or a FGFR ligand.

3. claims: 49-53 completely

use of a peptide sequence derived from an FGFR ligand for the preparation of a medicament for treatment of a disease or condition associated with or requiring activity of metallothionein and method of treatment of a condition or a disease associated with a deficiency of synthesis or function of metallothionein.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/DK2007/000152

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03105910	A	24-12-2003	EP 1531905 A1	25-05-2005
			NZ 537103 A	30-11-2007
			US 2005130888 A1	16-06-2005
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			EP 1434798 A2	07-07-2004
			JP 2005510463 T	21-04-2005
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			CN 101027320 A	29-08-2007
			EP 1765861 A2	28-03-2007