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- with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:

13 June 2013

(54) Title: NOVEL SEQUENCES FOR THE CONTROL OF REPRODUCTION IN FISH

(57) Abstract: The present invention relates to novel peptide sequences, compositions and methods for controlling fish reproduc-
tion. More particularly, the invention provides novel Neurokinin B peptides NKF and NKB and analogues thereof that regulate re-
production in fish. The invention further provides preprohormone thereof comprising at least one of a first peptide fragment of the
amino acid sequence X¹-X²-X³-X⁴-X⁵-X⁶-Asp⁷-X⁸-Phe⁹-Val¹⁰-X¹¹-Leu¹²-Met¹³ and a second peptide fragment of the
amino acid sequence of Glu¹-Met²-His³-Asp⁴-Ile⁵-Phe⁶-Val⁷-Gly⁸-Leu⁹-Met¹⁰ and variants thereof, nucleic acid sequences and novel
fish NKB receptors.



INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2012/050287

A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61K38/22 C07K14/47 C07K14/575
 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)

A61K 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 practicable, search terms used)

EPO-Internal , BIOSIS, EMBASE, WPI Data, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE Uni Prot [Onl i ne] 5 April 2011 (2011-04-05) , "SubName: Full=Preprotachykinin 2a; SubName: Fulltachykinin 3a; SubName: Full=Uncharacterized protein; ", XP002691255, retrieved from EBI accession no. UNIPROT: E9QE01 Database accession no. E9QE01 sequence ----- -/- .	1-32



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 application or patent 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

30 January 2013

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INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2012/050287

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL [Onl i ne] 8 October 2009 (2009-10-08) , "R_Platel2_74_B10 Fathead minnow brain cDNA Library Pimephales promelas cDNA 5' , mRNA sequence. " , XP002691256, retrieved from EBI accession no. EM_EST:GT146565 Database accession no. GT146565 sequence -----	22,23 , 31,32
X	DATABASE EMBL [Onl i ne] 3 March 2009 (2009-03-03) , "CBZA40150.bl CBZA: Normalized channel catfish cDNA library from stomach, muscle, olfactory tissue and trunk kidney (mixed tissue 2, AUL_M) Ictalurus punctatus cDNA 5' similar to zebrafish RefSeq, XP_706506.1, PREDICTED: hypothetical protein [Danio rerio], mRNA sequence. " , XP002691257 , retrieved from EBI accession no. EM_EST:GH667811 Database accession no. GH667811 sequence -----	22,23 , 31,32
X	DATABASE EMBL [Onl i ne] 31 May 2008 (2008-05-31) , "Dicentrarchus labrax EST, clone CDN30P0007015, 5'-end sequence" , XP002691258, retrieved from EBI accession no. EM_EST:FM019539 Database accession no. FM019539 sequence -----	22,23 , 31,32
X	DATABASE EMBL [Onl i ne] 3 November 2005 (2005-11-03) , "Oryzias latipes EST, clone McF0054018-MGRbd" , XP002691259 , retrieved from EBI accession no. EM_EST:AM154728 Database accession no. AM154728 sequence ----- -/--	22,23 , 31,32

INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2012/050287

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL [Onl i ne] 2 July 2008 (2008-07-02) , "K055E07 Antarcti c f i sh Di ssosti chus mawsoni adul t headki dney l i brary Di ssosti chus mawsoni cDNA, mRNA sequence. ", XP002691260, retri eved from EBI accessi on no. EM_EST: FE208182 Database accessi on no. FE208182 sequence -----	22,23 , 31,32
X	DATABASE EMBL [Onl i ne] 30 August 2007 (2007-08-30) , "EST_sras_evg_780996 srasevg mi xed_t i ssue Sebastes rastrel l i ger cDNA Sebastes rastrel l i ger cDNA clone sras_evg_503_84_rev 3', mRNA sequence. ", XP002691261 , retri eved from EBI accessi on no. EM_EST: EW979882 Database accessi on no. EW979882 sequence -----	22,23 , 31,32
X	DATABASE EMBL [Onl i ne] 1 November 2007 (2007-11-01) , "znc_0030_E12 Gadus morhua i ntesti nal l i brary ZNC Gadus morhua cDNA, mRNA sequence. ", XP002691262 , retri eved from EBI accessi on no. EM_EST: EX741313 Database accessi on no. EX741313 sequence -----	22,23 , 31,32
X	DATABASE EMBL [Onl i ne] 4 July 2010 (2010-07-04) , "EST_bsai_evw_1261517 bsai evw whol e Boreogadus sai da cDNA Boreogadus sai da cDNA clone bsai_evw_017_299 5', mRNA sequence. ", XP002691263 , retri eved from EBI accessi on no. EM_EST: H0077860 Database accessi on no. H0077860 sequence ----- -/--	22,23 , 31,32

INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2012/050287

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL [Onl i ne] 1 June 2007 (2007-06-01) , "Ami SEST003426 Juveni le Ameri can Alligator Liver Li brary (NIBB, Japan) Alligator mi ssi ssi ppi ensi s cDNA clone KTU01-S-CLT-C-000001D03 simi lar to best hit in human is TAC3 Isoform 1 of Neuroki nin-B precursor, mRNA sequence. ", XP002691264, retri eved from EBI accessi on no. EM_EST: ES319059 Database accessi on no. ES319059 sequence	22,23 , 31,32
X	----- SARANG M K ET AL: "Effect of pi sci ne GH/IGF-I on final oocyte maturati on in vitro in Heteropneustes fossi lis", FISH PHYSIOLOGY AND BIOCHEMISTRY, KLUWER ACADEMIC PUBLISHERS, DO, vol . 31, no. 2-3 , 1 Apri l 2005 (2005-04-01) , pages 231-233 , XP019748407 , ISSN: 1573-5168, DOI : 10. 1007/S10695-006-0029-Y the whol e document	1-7
X, P	----- BI RAN JAKOB ET AL: "Neuroki nin Bs and neuroki nin B receptors in zebraf ish-potenti al rol e in control ling fish reproducti on.", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 26 JUN 2012 , vol . 109, no. 26, 26 June 2012 (2012-06-26) , pages 10269-10274, XP002691265 , ISSN: 1091-6490 the whol e document -----	1-44

INTERNATIONAL SEARCH REPORT

International application No.
PCT/I L2G12/050287

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. 1-3, 6-21, 23-44(al l parti al ly)
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:
see FURTHER INFORMATION sheet PCT/ISA/210

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:

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1-3, 6-21, 23-44(al l parti al ly)

Present claims 1-3, 6-21 and 23-44 relate to an extremely large number of possible compounds. Support and disclosure in the sense of Article 6 and 5 PCT is to be found however for only a very small proportion of the compounds claimed, namely the polypeptides of SEQ ID No. 49, 52, 56, 60, 67, 71, 75, 79, 81, 83, 85, 87, 89 and 91, and the polynucleotides of SEQ ID No. 4, 5, 51, 55, 59, 63, 66, 70, 74, 78, 80, 82, 84, 86, 88 and 90. The non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of claims 1-3, 6-21 and 23-44 (PCT Guidelines 9.19 and 9.23). The search of claims 1-3, 6-21 and 23-44 was restricted to those claimed compounds which appear to be supported.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.2), should the problems which led to the Article 17(2) declaration be overcome.