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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :		(11) International Publication Number:	WO 00/23464
C12N 15/10, C07K 14/47	A3	(43) International Publication Date:	27 April 2000 (27.04.00)

(21) International Application Number: PCT/EP99/07742

(22) International Filing Date: 14 October 1999 (14.10.99)

(30) Priority Data:
09/173,941 16 October 1998 (16.10.98) US

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(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(88) Date of publication of the international search report:
16 November 2000 (16.11.00)

(54) Title: ZINC FINGER BINDING DOMAINS FOR GNN

(57) Abstract

Zinc finger–nucleotide binding polypeptides having binding specificity for target nucleotides containing one or GNN triplets are provided. Compositions containing such polypeptides and the use of such polypeptides and compositions for regulating nucleotide function are also provided.

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INTERNATIONAL SEARCH REPORT

Interna al Application No
PCT/EP 99/07742

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/10 C07K14/47

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 C12N 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	T. OGAWA ET AL.,: "Enhanced expression in seminoma of human zinc finger genes located on chromosome 19" CANCER GENET. CYTOGENET., vol. 100, no. 1, 1 January 1998 (1998-01-01), pages 36-42, XP000882080 * page 37, right column, last full-paragraph; figure 1A * --- -/--	1-11, 19-21

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"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

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Date of the actual completion of the international search	Date of mailing of the international search report
27 March 2000	23. 06. 00

Name and mailing address of the ISA	Authorized officer
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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	B. GEBELEIN ET AL.,: "A novel profile of expressed tags for zinc finger encoding genes from the poorly differentiated exocrine pancreatic cell line AR4IP" CANCER LETT., vol. 105, no. 2, 2 August 1996 (1996-08-02), pages 225-231, XP000882088 * whole document, in particular Table 1 *	1-11, 19-21
A	CHOO Y ET AL: "Selection of DNA binding sites for zinc fingers using rationally randomized DNA reveals coded interactions" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA,US,NATIONAL ACADEMY OF SCIENCE. WASHINGTON, 8 November 1994 (1994-11-08), pages 1168-1172, XP002075339 ISSN: 0027-8424 cited in the application * whole document, in particular figure 1 and page 11172, left-column, last paragraph to right-column, last paragraph *	1-21
A	CHOO Y ET AL: "Toward a code for the interactions of zinc fingers with DNA: Selection of randomized fingers displayed on phage" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA,US,NATIONAL ACADEMY OF SCIENCE. WASHINGTON, 8 November 1994 (1994-11-08), pages 1163-1167, XP002075340 ISSN: 0027-8424 cited in the application * whole document, in particular figure 2 *	1-21
Y	WO 96 06166 A (MEDICAL RES COUNCIL ;CHOO YEN (SG); KLUG AARON (GB); GARCIA ISIDRO) 29 February 1996 (1996-02-29) * whole document, in particular Table 1 and figures 4 and 7 *	1-21
Y	Q. LIU ET AL.,: "Design of polydactyl zinc-finger proteins for unique addressing within complex genomes" PROC. NATL. ACAD. SCI. USA, vol. 94, May 1997 (1997-05), pages 5525-5530, XP002918175 cited in the application * whole document, in particular page 5529, right-column *	1-21

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INTERNATIONAL SEARCH REPORT

Int. .tional application No.
PCT/EP 99/07742

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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 II Observations where unity of invention is lacking (Continuation of item 2 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.:

1 - 21 (partial)

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

1. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 1; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 2-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 1; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

2. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 2; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1 or 3-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 2; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

3. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 3; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-2 or 4-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 3; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these

compositions; medicament comprising these compositions and uses thereof

4. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 4; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-3 or 5-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 4; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

5. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 5; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-4 or 6-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 5; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

6. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 6; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-5 or 7-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 6; an isolated and purified

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

7. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 7; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-6 or 8-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 7; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

8. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 8; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-7 or 9-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 8; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

9. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 9; compositions comprising from 2 to about 12 of isolated and purified zinc

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-8 or 10-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 9; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

10. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 10; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-9 or 11-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 10; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

11. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 11; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-10 or 12-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 11; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

12. Claims: 1-21 (partial)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 12; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-11 or 13-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 12; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

13. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 13; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-12 or 14-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 13; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

14. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 14; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-13 or 15-16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 14; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

compositions; medicament comprising these compositions and uses thereof

15. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 15; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-14 or 16 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 15; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

16. Claims: 1-21 (partial)

an isolated and purified zinc finger-nucleotide binding polypeptide that contains a nucleotide binding region having the sequence of SEQ ID No.: 16; compositions comprising from 2 to about 12 of isolated and purified zinc finger-nucleotide binding polypeptides containing the nucleotide binding regions having the sequence of any of SEQ ID No.: 1-15 and wherein at least one of said polypeptides contains the nucleotide binding region having the sequence of SEQ ID No.: 16; an isolated and purified polynucleotide encoding said polypeptide or compositions thereof; expression vectors; a process of regulating a nucleotide sequence that contains 5'-(GNN)n-3', where n is an integer from 1 to 6, the process comprising exposing the nucleotide sequence to an effective amount of these compositions; medicament comprising these compositions and uses thereof

INTERNATIONAL SEARCH REPORT

mation on patent family members

International Application No
PCT/EP 99/07742

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