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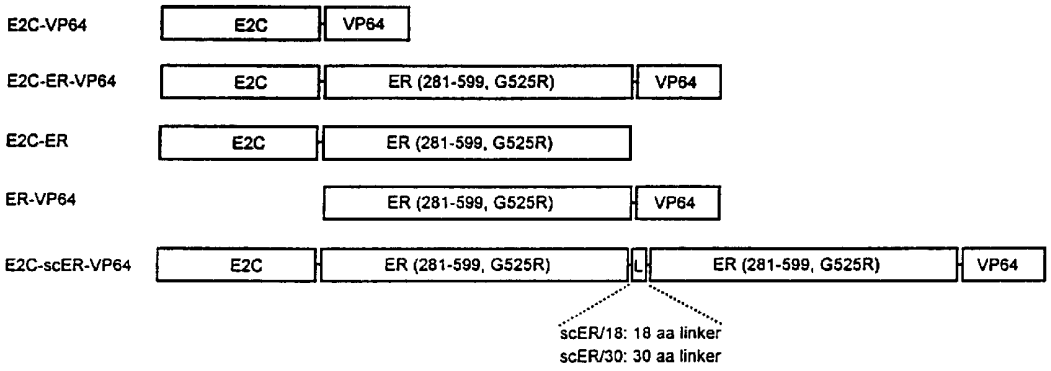
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(54) Title: REGULATION OF GENE EXPRESSION USING SINGLE-CHAIN, MONOMERIC, LIGAND DEPENDENT POLYPEPTIDE SWITCHES



(57) Abstract: Single chain, monomeric polypeptide gene switches are provided. The gene switches include ligand binding domains and at least one functional domain. Preferred functional domains are DNA binding domains and transcriptional regulating domains. Methods of regulating gene function using the switches are also provided.

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INTERNATIONAL SEARCH REPORT

Inte nal Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/12 C12N15/62 C12N15/63 C07K14/47 C07K14/72

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)
WPI Data, PAJ, CAB Data, SEQUENCE SEARCH, BIOSIS, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	BEERLI ROGER R ET AL: "Chemically regulated zinc finger transcription factors." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 275, no. 42, 20 October 2000 (2000-10-20), pages 32617-32627, XP002199787 ISSN: 0021-9258 the whole document ---	1-35
P,A	WO 01 30843 A (NOVARTIS AG ;SCRIPPS RESEARCH INST (US)) 3 May 2001 (2001-05-03) the whole document ---	
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
23 May 2002	07/06/2002

Name and mailing address of the ISA	Authorized officer
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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	BEERLI ROGER R ET AL: "Positive and negative regulation of endogenous genes by designed transcription factors" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 97, no. 4, 15 February 2000 (2000-02-15), pages 1495-1500, XP002188512 ISSN: 0027-8424 the whole document ---	
A	WO 99 10510 A (ARIAD GENE THERAPEUTICS INC ;GILMAN MICHAEL Z (US); NATESAN SRIDAR) 4 March 1999 (1999-03-04) page 25, line 28 -page 26, line 2 page 31, line 20 -page 33, line 2 claims 1,7,11-17; figures 1B,1D ---	
A	WO 98 18925 A (BAYLOR COLLEGE MEDICINE ;MALLEY BERT O (US); TSAI MING JER (US); T) 7 May 1998 (1998-05-07) the whole document ---	
A	EP 0 540 065 A (SALK INST FOR BIOLOGICAL STUDI) 5 May 1993 (1993-05-05) the whole document ---	
A	BURCIN M M ET AL: "A REGULATORY SYSTEM FOR TARGET GENE EXPRESSION" FRONTIERS IN BIOSCIENCE, XX, XX, vol. 3, 1 March 1998 (1998-03-01), pages 1-7, XP000874619 the whole document ---	
A	WO 00 23464 A (NOVARTIS ERFIND VERWALT GMBH ;NOVARTIS AG (CH); SCRIPPS RESEARCH I) 27 April 2000 (2000-04-27) cited in the application the whole document ---	
A	WO 99 47656 A (MEDICAL RES COUNCIL ;ISALAN MARK (GB); CHOO YEN (GB)) 23 September 1999 (1999-09-23) the whole document -----	

INTERNATIONAL SEARCH REPORT

Inte nal Application No
PCT/EP 01/08190

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0130843 A	03-05-2001	AU 1143801 A	08-05-2001
		WO 0130843 A1	03-05-2001
WO 9910510 A	04-03-1999	US 6015709 A	18-01-2000
		WO 9910508 A1	04-03-1999
		AU 9036198 A	16-03-1999
		CA 2300376 A1	04-03-1999
		EP 1017829 A2	12-07-2000
		WO 9910510 A2	04-03-1999
		US 6117680 A	12-09-2000
		US 2002048792 A1	25-04-2002
		AU 4240297 A	16-03-1999
		CA 2303482 A1	04-03-1999
		EP 1003886 A1	31-05-2000
		JP 2001514007 T	11-09-2001
WO 9818925 A	07-05-1998	AU 6908998 A	22-05-1998
		EP 0935657 A2	18-08-1999
		JP 2001504690 T	10-04-2001
		WO 9818925 A2	07-05-1998
EP 0540065 A	05-05-1993	US 4981784 A	01-01-1991
		EP 0540065 A1	05-05-1993
		AT 124721 T	15-07-1995
		AT 182685 T	15-08-1999
		AU 628312 B2	17-09-1992
		AU 2818889 A	05-07-1989
		AU 665039 B2	14-12-1995
		AU 3026892 A	22-04-1993
		DE 3854120 D1	10-08-1995
		DE 3856354 D1	02-09-1999
		DE 3856354 T2	16-12-1999
		DK 136890 A	01-06-1990
		EP 0325849 A2	02-08-1989
		ES 2073408 T3	16-08-1995
		IE 68590 B1	26-06-1996
		JP 10295385 A	10-11-1998
		JP 10279599 A	20-10-1998
		JP 3006716 B2	07-02-2000
		JP 3503597 T	15-08-1991
		KR 9709951 B1	19-06-1997
		WO 8905355 A1	15-06-1989
		US 5571692 A	05-11-1996
		US 5548063 A	20-08-1996
		US 5171671 A	15-12-1992
		US 5599904 A	04-02-1997
		US 5274077 A	28-12-1993
WO 0023464 A	27-04-2000	US 6140081 A	31-10-2000
		AU 1037600 A	08-05-2000
		BR 9914599 A	13-11-2001
		CN 1330713 T	09-01-2002
		WO 0023464 A2	27-04-2000
		EP 1121381 A2	08-08-2001
WO 9947656 A	23-09-1999	AU 2944999 A	11-10-1999
		CA 2323064 A1	23-09-1999
		EP 1064369 A2	03-01-2001

INTERNATIONAL SEARCH REPORT

Inte nal Application No
PCT/EP 01/08190

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9947656 A		WO 9947656 A2	23-09-1999
		JP 2002506640 T	05-03-2002