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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, 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, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, 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, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG)*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, 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, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, 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, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG)*

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(54) Title: ECDYSONE RECEPTOR-BASED INDUCIBLE GENE EXPRESSION SYSTEM

(57) Abstract: This invention relates to the field of biotechnology or genetic engineering. Specifically, this invention relates to the field of gene expression. More specifically, this invention relates to a novel inducible gene expression system and methods of modulating gene expression in a host cell for applications such as gene therapy, large scale production of proteins and antibodies, cell-based high throughput screening assays, functional genomics and regulation of traits in transgenic plants and animals.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/63 C12N15/85 C12N15/12 C12N15/62 C07K14/705
C07K14/72 A01H5/00 C12Q1/68 G01N33/68

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 C07K C12N A01H C12Q G01N

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.
X	WO 96 27673 A (CIBA GEIGY AG) 12 September 1996 (1996-09-12) cited in the application page 12, paragraph 3 -page 13, paragraph 2; claims 10,12-16,18-20; figure 3; examples 3,4,8,10,19; tables 4-6 --- -/--	1-32, 47-71

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

[X] Patent family members are listed in annex.

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28 May 2002	13/06/2002
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Smalt, R

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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.
X	CHRISTOPHERSON K S ET AL: "ECDYSTEROID-DEPENDENT REGULATION OF GENES IN MAMMALIAN CELLS BY A DROSOPHILA ECDYSONE RECEPTOR AND CHIMERIC TRANSACTIVATORS" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 89, July 1992 (1992-07), pages 6314-6318, XP002921831 ISSN: 0027-8424 the whole document	1-32, 48-71
X	WO 99 10510 A (ARIAD GENE THERAPEUTICS INC ;GILMAN MICHAEL Z (US); NATESAN SRIDAR) 4 March 1999 (1999-03-04) claims 8,10,12,27,29,30,33,34,36,53	1-32, 48-71
X	WO 99 58155 A (EVANS ROLAND M ;SAEZ ENRIQUE (US); SALK INST FOR BIOLOGICAL STUDI) 18 November 1999 (1999-11-18) figure 1D	1-32, 42-71
X	KAKIZAWA TOMOKO ET AL: "Ligand-dependent heterodimerization of thyroid hormone receptor and retinoid X receptor." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 272, no. 38, 1997, pages 23799-23804, XP002200320 ISSN: 0021-9258 see whole document, particularly figure 1	1-6, 9-14, 17-21, 27,28, 31,32, 48-71
X	PERERA SRINI C ET AL: "An analysis of ecdysone receptor domains required for heterodimerization with ultraspiracle." ARCHIVES OF INSECT BIOCHEMISTRY AND PHYSIOLOGY, vol. 41, no. 2, 1999, pages 61-70, XP001077866 ISSN: 0739-4462 the whole document	33-35, 42-45
A	WO 99 02683 A (GAGE FRED H ;SUHR STEVEN T (US); SALK INST FOR BIOLOGICAL STUDI (U) 21 January 1999 (1999-01-21) cited in the application page 22, paragraph 2; examples 1,10,14	

-/--

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	KOELLE M R ET AL: "THE DROSOPHILA ECR GENE ENCODES AN ECDYSONE RECEPTOR, A NEW MEMBER OF THE STEROID RECEPTOR SUPERFAMILY" CELL, CELL PRESS, CAMBRIDGE, NA, US, vol. 67, no. 1, 4 October 1991 (1991-10-04), pages 59-77, XP001010154 ISSN: 0092-8674 the whole document	
A	LEID M ET AL: "PURIFICATION, CLONING, AND RXR IDENTITY OF THE HELA CELL FACTOR WITH WHICH RAR OR TR HETERODIMERIZES TO BIND TARGET SEQUENCES EFFICIENTLY" CELL, CELL PRESS, CAMBRIDGE, NA, US, vol. 68, 24 January 1992 (1992-01-24), pages 377-395, XP002007203 ISSN: 0092-8674 the whole document	
A	PERERA SRINI C ET AL: "Studies on two ecdysone receptor isoforms of the spruce budworm, Choristoneura fumiferana." MOLECULAR AND CELLULAR ENDOCRINOLOGY, vol. 152, no. 1-2, 25 June 1999 (1999-06-25), pages 73-84, XP002200321 ISSN: 0303-7207 the whole document	
A	EP 0 798 378 A (AKZO NOBEL NV) 1 October 1997 (1997-10-01) the whole document	
A	EP 0 965 644 A (ROHM & HAAS) 22 December 1999 (1999-12-22) the whole document	

INTERNATIONAL SEARCH REPORT

nformation on patent family members

Ir ıtional Application No
PCT/US 01/09050

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9627673 A	12-09-1996	AU 703124 B2	18-03-1999
		AU 4878296 A	23-09-1996
		CA 2213340 A1	12-09-1996
		WO 9627673 A1	12-09-1996
		EP 0813604 A1	29-12-1997
		HU 9800353 A2	28-05-1998
		JP 11500922 T	26-01-1999
		US 5880333 A	09-03-1999
		US 6147282 A	14-11-2000
		US 2001022004 A1	13-09-2001
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 9958155 A	18-11-1999	US 6333318 B1	25-12-2001
		AU 3648699 A	29-11-1999
		CA 2328521 A1	18-11-1999
		EP 1076569 A1	21-02-2001
		WO 9958155 A1	18-11-1999
WO 9902683 A	21-01-1999	US 6300488 B1	09-10-2001
		AU 738494 B2	20-09-2001
		AU 8389598 A	08-02-1999
		EP 0998560 A1	10-05-2000
		WO 9902683 A1	21-01-1999
		US 2002048815 A1	25-04-2002
EP 0798378 A	01-10-1997	EP 0798378 A2	01-10-1997
		EP 1162264 A2	12-12-2001
		GR 98300076 T1	30-11-1998
		AT 212055 T	15-02-2002
		AU 715812 B2	10-02-2000
		AU 1652197 A	02-10-1997
		CA 2200423 A1	26-09-1997
		DE 69709561 D1	21-02-2002
		DE 798378 T1	04-03-1999
		DK 798378 T3	29-04-2002
		ES 2123482 T1	16-01-1999
		HU 9700636 A2	28-04-1998
		JP 10004986 A	13-01-1998
EP 0965644 A	22-12-1999	US 6258603 B1	10-07-2001
		AU 3390099 A	10-02-2000
		BR 9902283 A	02-05-2000
		CN 1251389 A	26-04-2000
		EP 0965644 A2	22-12-1999
		JP 2000037189 A	08-02-2000
		US 2001044151 A1	22-11-2001