

US008101823B2

(12) United States Patent

Werner et al.

(10) Patent No.: US 8,101,823 B2 (45) Date of Patent: Jan. 24, 2012

(54) METHOD OF CONTROLLING A CELLULAR PROCESS IN A MULTI-CELLULAR ORGANISM

(75) Inventors: Stefan Werner, Halle/Saale (DE);
Sylvestre Marillonnet, Halle/Saale
(DE); Yurii Dorokhov, Moscow (RU);
Victor Klimyuk, Halle/Saale (DE); Yuri
Gleba, Halle/Saale (DE)

(73) Assignee: Icon Genetics GmbH, München (DE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35

U.S.C. 154(b) by 324 days.

(21) Appl. No.: 10/535,763

(22) PCT Filed: Nov. 20, 2003

(86) PCT No.: **PCT/EP03/13021**

§ 371 (c)(1),

(2), (4) Date: May 20, 2005

(87) PCT Pub. No.: **WO2004/046361**

PCT Pub. Date: Jun. 3, 2004

(65) **Prior Publication Data**

US 2006/0075524 A1 Apr. 6, 2006

(30) Foreign Application Priority Data

Nov. 20, 2002 (EP) 10254165

(51) Int. Cl. C12N 15/82 (2006.01) C12N 15/29 (2006.01) C12N 15/00 (2006.01) A01H 5/00 (2006.01)

(52) **U.S. Cl.** **800/294**; 800/278; 800/288; 800/295; 435/320.1; 435/468; 536/23.1; 536/23.2;

(56) References Cited

U.S. PATENT DOCUMENTS

2002/0046419 A1 4/2002 Choo et al. 2002/0143142 A1 10/2002 Lin et al.

FOREIGN PATENT DOCUMENTS

JP 2000-500323 1/2000 WO WO 95/21248 A1 8/1995

VO	WO9521248	*	8/1995
VO	WO 98/37211		8/1998
VO	WO 99/52563 A1		10/1999
VO	WO0071701	*	5/2000
VO	WO 00/52146 A2		9/2000
VO	WO 00/52146 A3		9/2000
VO	WO 00/71701 A1		11/2000
VO	WO 01/38488 A2		5/2001
VO	WO0189283	*	5/2001
VO	WO0189283	×	11/2001

OTHER PUBLICATIONS

Mackenzie 2005 Trends in Cell Biology 15:548-554.*

Jo, E., et al., "Epigenetic Regulation of Gene Structure and Function with a Cell-Permeable Cre Recombinase," *Nature Biotechnology*, 2001, pp. 929-933, vol. 19, Nature Publishing Group.

Will, E., et al., "Unmodified Cre Recombinase Crosses the Membrane," *Nucleic Acids Research*, 2002, pp. 1-6, vol. 30(12)e59, Oxford University Press.

Zhang, Y., et al., "Efficient and Inducible Production of Human Interleukin 6 in Chinese Hamster Ovary Cells Using a Novel Expression System," *Cytotechnology*, 1997, pp. 53-60, vol. 25, Kluwer Academic Publishers, Netherlands.

O'Donnell, P., et al., "A Novel Tomato Gene that Rapidly Responds to Wound- and Pathogen-Related Signals," *The Plant Journal*, 1998, pp. 137-142, vol. 14(1), Blackwell Science Ltd.

Pearce, G., et al., "A Polypeptide from Tomato Leaves Induces Wound-Inducible Proteinase Inhibitor Proteins," *Science Reports*, 1991, pp. 895-898, vol. 23.

Thyagarajan, B., et al., "Mammalian genomes contain active recombinase sites," *Gene*, 2000, vol. 244, pp. 47-54.

Schmidt, E., et al., "Illegitimate Cre-dependent chromosome rearrangements in transgenic mouse spermatids," *PNAS*, 2000, vol. 97(25), pp. 13702-13707.

"Chemistry of Organisms—Chemistry in Treating Diseases from Gene Therapy to Protein Therapy," *Chemistry*, 2002, vol. 57(9), pp.

Gelvin, Stanton B., *Agrobaterium*-Mediated Plant Transformation: the Biology behind the "Gene-Jockeying" Tool, Microbiology and Molecular Biology Reviews, Mar. 2003, vol. 67, No. 1, p. 16-37.

* cited by examiner

Primary Examiner — Brent T Page (74) Attorney, Agent, or Firm — Alston & Bird LLP

(57) ABSTRACT

A method of controlling a genetically-modified multi-cellular organism or a part thereof, comprising the following steps:
(a) providing a multi-cellular organism or a part thereof, whereby cells of said multi-cellular organism or said part contain a heterologous nucleic acid, (b) causing expression of a I protein from said heterologous nucleic acid in at least some of said cells, wherein said protein is capable of (i) leaving a cell and entering other cells of said multi-cellular organism or a part thereof, (ii) causing expression of said protein in cells containing said heterologous nucleic acid, and optionally (iii) controlling a cellular process of interest.

11 Claims, 8 Drawing Sheets