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ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: GENETIC MODIFICATION OF SOMATIC CELLS AND USES THEREOF

(57) Abstract: The production of genetically modified animals, in which the genetic modifications are engineered in somatic cells cultured *in vitro* by gene targeting, is described. Genetically modified cells may then be used as nuclear donors loci in animal chromosomes which are suitable sites for transgene addition to cells.



WO 00/51424 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/00778

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/10 C12N15/90 C12N15/88 C12N5/06 A01K67/027

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 A01K

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.
P,X	POLEJAEVA, I.A. AND CAMPBELL, K.H.S.: "New advances in somatic cell nuclear transfer: Application in transgenesis" THERIOGENOLOGY, vol. 53, no. 1, 1 January 2000 (2000-01-01), pages 117-126, XP000940942 the whole document	1-6, 9-12,14, 16-26, 29-34, 37-40, 43,45
X	WO 98 37183 A (PPL THERAPEUTICS (SCOTLAND) LIMITED) 27 August 1998 (1998-08-27) page 14, line 10 -page 27, line 25 page 28, line 27 -page 30, line 5; examples 2-6 --- -/--	1-6, 8-10, 12-34, 36-38, 40-45

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in 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 document 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

7 November 2000

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09.01.01

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INTERNATIONAL SEARCH REPORT

International Application No

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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	WO 98 30683 A (UNIVERSITY OF MASSACHUSETTS) 16 July 1998 (1998-07-16) cited in the application page 10, line 5 -page 16, line 15 page 18, line 17 -page 24, line 22; examples 1,2 ---	1,3-6,9, 10,13, 14, 16-29, 31-34, 37,38, 41-43,45
X	WO 97 07668 A (ROSLIN INSTITUTE (EDINBURGH)) 6 March 1997 (1997-03-06) cited in the application page 5, line 1 -page 7, line 25 page 8, line 24 - line 27 page 15, line 15 -page 16, line 7 page 18, line 18 - line 22 ---	1,3-6, 9-11,13, 14, 16-29, 31-34, 37-39, 41-43,45
X	WO 97 07669 A (ROSLIN INSTITUTE (EDINBURGH)) 6 March 1997 (1997-03-06) cited in the application page 3, line 29 -page 7, line 33 page 15, line 7 -page 17, line 16 page 19, line 29 -page 20, line 26 ---	1,3-6, 9-11,13, 14, 16-29, 31-34, 37-39, 41-43,45
X	SCHNIEKE, A.E. ET AL.: "Human factor IX transgenic sheep produced by transfer of nuclei from transfected fetal fibroblasts" SCIENCE, vol. 278, 19 December 1997 (1997-12-19), pages 2130-2133, XP002067036 cited in the application the whole document ---	1,3-6,8, 11,13, 14, 16-26, 29, 31-34, 36,39, 41-43,45
X	CIBELLI, J.B. ET AL.: "Embryonic stem cells: Bovine chimeric offspring produced by transgenic embryonic stem cells generated from somatic cell nuclear transfer embryos" ANNUAL CONFERENCE OF THE INTERNATIONAL EMBRYO TRANSFER SOCIETY, vol. 49, no. 1, 18 January 1998 (1998-01-18), page 236 XP000764040 the whole document ---	1,3-5, 14, 16-29, 31-33, 42,43,45

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/00778

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ROBL. J.M. ET AL.: "Somatic cell nuclear transplantation in cattle" ANNUAL MEETING SOC. STUDY REPROD, vol. 58, 8 August 1998 (1998-08-08), page 25 XP000791151 the whole document ---	1-45
Y	WO 98 56903 A (PRESIDENT AND FELLOWS OF HARVARD COLLEGE) 17 December 1998 (1998-12-17) the whole document ---	1-45
A	CAMPBELL, K.H.S. AND WILMUT, I.: "Totipotency or multipotentiality of cultured cells: Applications and progress" THERIOGENOLOGY, vol. 47, 1997, pages 63-72, XP000940776 the whole document ---	1-45
A	WAKAYAMA, T. ET AL.: "Full-term development of mice from enucleated oocytes injected with cumulus cell nuclei" NATURE, vol. 394, 23 July 1998 (1998-07-23), pages 369-374, XP002900702 cited in the application the whole document ---	1-45
T	MCCREATH, K.J. ET AL.: "Production of gene-targeted sheep by nuclear transfer from cultured somatic cells" NATURE, vol. 405, 29 July 2000 (2000-07-29), pages 1066-1069, XP000919025 the whole document -----	1-45

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 00/00778

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:

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.:

1-45

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: 1-45

Claims 1-45 refer to a method of preparing a somatic cell for nuclear transfer comprising modifying the genetic material of the somatic cell by a genetic targeting event, to a method of nuclear transfer comprising the transfer of the genetic material from said modified somatic cell to a recipient cell, to a transgenic embryo obtained by said method of nuclear transfer and to a transgenic animal developed to term from said embryo.

2. Claims: 46-50

Claims 46-50 refer to the general use of artificial induction of gene expression or induction of chromatin changes in the genetic targeting of a cell.

3. Claims: 51-55

Claims 51 - 55 refer to the use of an animal, which has been obtained in general from a cell following a genetic targeting event.

4. Claims: 56-61

Claims 56 - 61 refer to a general method for validating a locus for targeted gene therapy and to the validated locus obtained by said method.

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/GB 00/00778

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