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62/767,373	14 November 2018 (14.11.2018)	US
62/806,594	15 February 2019 (15.02.2019)	US

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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(54) Title: SYSTEMS AND METHODS FOR NONDESTRUCTIVE TESTING OF GAMETES

(57) Abstract: This disclosure provides, e.g., methods of physically separating sperm carrying a first allele of a phenotype-associated site (e.g., a non-disease allele) from sperm carrying a second allele (e.g., a disease allele). The methods can include separating the sperm cells into two populations based on a heterozygous geno-informative marker site that is genetically linked to the phenotype-associated site.



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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
- a. ☐ forming part of the international application as filed:
- ☐ in the form of an Annex C/ST.25 text file.
- ☐ on paper or in the form of an image file.
- b. ☐ furnished together with the international application under PCT Rule 13~~ter~~.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
- c. ☒ furnished subsequent to the international filing date for the purposes of international search only:
- ☒ in the form of an Annex C/ST.25 text file (Rule 13~~ter~~.1(a)).
- ☐ on paper or in the form of an image file (Rule 13~~ter~~.1(b) and Administrative Instructions, Section 713).
2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 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 No. III Observations where unity of invention is lacking (Continuation of item 3 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 fees, this Authority did not invite payment of additional fees.
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, 4-6

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

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International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N5/071
ADD.

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)
C12N

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 practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2014/359795 A1 (FAHRENKRUG SCOTT C [US] ET AL) 4 December 2014 (2014-12-04) abstract; [0042]ff.; claim 22; [0088]ff. -----	4
X	US 2013/130263 A1 (VEGA MANUEL [FR] ET AL) 23 May 2013 (2013-05-23) abstract; [0018], [0046]ff., [0089]ff., [0115]ff., [0135]ff.; claim 21; fig 1 -----	4,5
X	WO 2005/043991 A1 (BABRAHAM INST [GB]; SAUNDERS JOHN C [GB]) 19 May 2005 (2005-05-19) p 8, 3rd full paragraph; p 3, 1st full paragraph; p 12, l 30 to p 13, l 7; p 13, l 31 to p 14, l 3; p 17, l 24ff.; claim 32 ----- -/-	4



Further documents are listed in the continuation of Box C.



See patent family 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 application or patent 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

12 March 2020

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26/06/2020

Name and mailing address of the ISA/

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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 2010/120518 A2 (BIOCERN INC [US]; OKSENBERG DAVID A [US]) 21 October 2010 (2010-10-21) abstract; [0222]ff., [0240], [0262], [0273]; claims 6 and 7 -----	4
A	SHIV KUMAR YADAV ET AL: "An immunological approach of sperm sexing and different methods for identification of X- and Y-chromosome bearing sperm", VETERINARY WORLD, vol. 10, no. 5, 1 May 2017 (2017-05-01), pages 498-504, XP055675617, India ISSN: 0972-8988, DOI: 10.14202/vetworld.2017.498-504 abstract; p 499-500 -----	1,4-6
A	WO 01/42283 A2 (UNIV GUELPH [CA]; BLECHER STAN R [CA]; DETMAR JACQUELINE [CA]) 14 June 2001 (2001-06-14) the whole document -----	1,4-6
T	Kunal Bhutani ET AL: "Widespread haploid-biased gene expression in mammalian spermatogenesis associated with frequent selective sweeps and evolutionary conflict", bioRxiv, 18 November 2019 (2019-11-18), XP055675625, DOI: 10.1101/846253 Retrieved from the Internet: URL: http://biorxiv.org/lookup/doi/10.1101/846253 [retrieved on 2020-03-11] the whole document -----	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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		WO 0142283 A2	14-06-2001

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1, 4-6

A method of selecting a sperm cell according to claim 1; and subject-matter relating thereto.

2. claims: 2, 7

A method of producing a fertilized egg according to claims 2 and 7.

3. claim: 3

A method of producing a fertilized egg or preventing fertilization by a sperm cell according to claim 3.
