

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization

International Bureau

(43) International Publication Date
24 May 2018 (24.05.2018)



(10) International Publication Number
WO 2018/090991 A1

(51) International Patent Classification:
C12Q 1/68 (2006.01)

(21) International Application Number:
PCT/CN2017/111843

(22) International Filing Date:
20 November 2017 (20.11.2017)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/424,088 18 November 2016 (18.11.2016) US

(71) Applicant: THE CHINESE UNIVERSITY OF HONG KONG [CN/CN]; Room 301, Pi Ch'iu Building, Office of Research and Knowledge Transfer Services, Shatin, New Territories, Hong Kong 999077 (CN).

(72) Inventors: HUI, Wai In; Flat 11, 31/F, Block E, Lung Poon Court, Diamond Hill, Kowloon, Hong Kong (CN). JIANG, Peiyong; Flat 7 on 1st Floor of Block B of Kwong Lam Court, Nos. 62-66 (No.62) Siu Lek Yuen Road, Shatin, New Territories, Hong Kong 999077 (CN). CHAN, Kwan Chee; Flat C, 15th Floor, Block 5, Peak One, Mei Tin Road, Shatin, New Territories, Hong Kong 999077 (CN). LO, Yuk-Ming Dennis; 4th Floor, 7 King Tak Street, Homan-tin, Kowloon, Hong Kong 999077 (CN). CHIU, Rossa Wai Kwun; House 31, Double Haven, 52 Ma Lok Path, Shatin, New Territories, Hong Kong 999077 (CN).

(74) Agent: INSIGHT INTELLECTUAL PROPERTY LIMITED; 19 A, Tower A, InDo Building, No. 48A Zhichun Road, Haidian District, Beijing 100098 (CN).

(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.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))



WO 2018/090991 A1

(54) Title: UNIVERSAL HAPLOTYPE-BASED NONINVASIVE PRENATAL TESTING FOR SINGLE GENE DISEASES

(57) Abstract: To detect a fetal mutation inherited from the mother without paternal genetic information, a property of each maternal haplotype can be measured in the cell-free mixture. A separation value between values of the property for the two maternal haplotypes can be compared to thresholds to determine which haplotype is inherited. As measurements of a paternal allele may not be available, embodiments can measure the property at some loci where the fetus is homozygous and some loci where the fetus is heterozygous, but account for such loci where the fetus is heterozygous in the selection of a threshold for determining inheritance of a maternal haplotype. To determine parental haplotypes, direct haplotyping can be performed, and loci within a specified of the mutation can be selected and used in haplotype block for the measurements. Targeted measurements of a region including the mutation using predetermined primer/probes that may be re-used across subjects.