



- (51) **International Patent Classification:**
G16B 30/00 (2018.01) *G16B 20/00* (2019.01)
- (21) **International Application Number:**
PCT/US2019/022504
- (22) **International Filing Date:**
15 March 2019 (15.03.2019)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
62/643,649 15 March 2018 (15.03.2018) US
62/769,928 20 November 2018 (20.11.2018) US
- (71) **Applicant:** **GRAIL, INC.** [US/US]; 1525 O'Brien Drive, Menlo Park, CA 94025 (US).
- (72) **Inventors:** **LO, Yuk-Ming, Dennis;** 4/F, 7 King Tak Street, Homantin, Kowloon, Hong Kong (CN). **CHIU, Rossa, Wai Kwun;** House 31, Double Haven, 52 Ma Lok Path, Shatin, New Territories, Hong Kong (CN). **CHAN, Kwan, Chee;** 15C, Block 5, Peak One, Shatin, New Territories, Hong

Kong (CN). **GAI, Wanxia;** Room 403, Li Ka Shing Medical Sciences Building, Shatin, New Territories, Hong Kong (CN). **Ji, Lu;** Room 503, Li Ka Shing Medical Sciences Building, Shatin, New Territories, Hong Kong (CN).

- (74) **Agent:** **HUANG, Wei;** Wilson Sonsini Goodrich & Rosati, 650 Page Mill Road, Palo Alto, CA 94304 (US).

- (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,

(54) **Title:** TISSUE-SPECIFIC METHYLATION MARKER

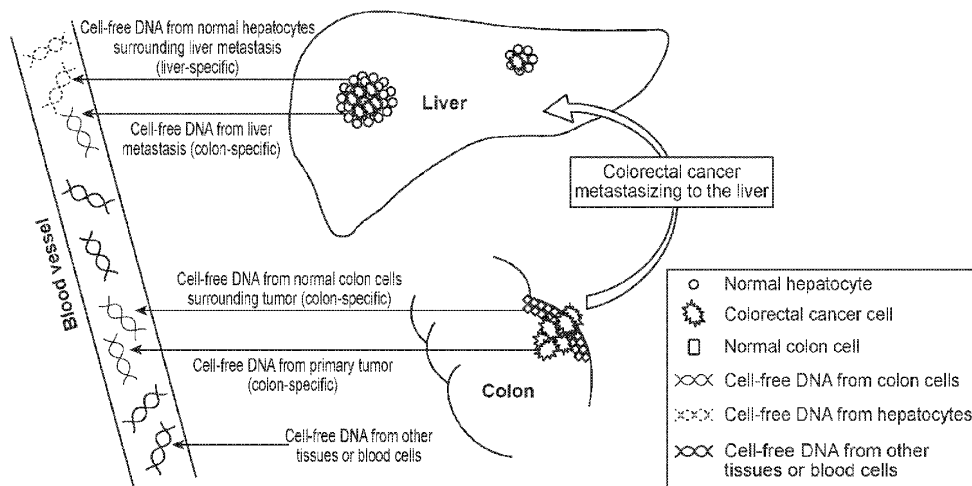


FIG. 1

(57) **Abstract:** Provided herein are compositions comprising tissue-specific markers for identifying a tissue of origin of a cell-free nucleic acid, e.g., a cell-free DNA molecule. Also provided herein are methods, compositions, and systems for identifying a tissue of origin of a cell-free nucleic acid by determining an absolute amount of cell-free nucleic acids comprising the tissue-specific marker. Also provided herein are methods, compositions, and systems for detecting a cancer in a tissue of an organism by analyzing tissue-specific markers.

[Continued on next page]

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))*
- *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))*