



(51) International Patent Classification:
C12Q 1/68 (2018.01) *G06F 19/10* (2011.01)

(21) International Application Number:
PCT/IB2017/054231

(22) International Filing Date:
13 July 2017 (13.07.2017)

(25) Filing Language: Italian

(26) Publication Language: English

(30) Priority Data:
102017000045353 26 April 2017 (26.04.2017) IT

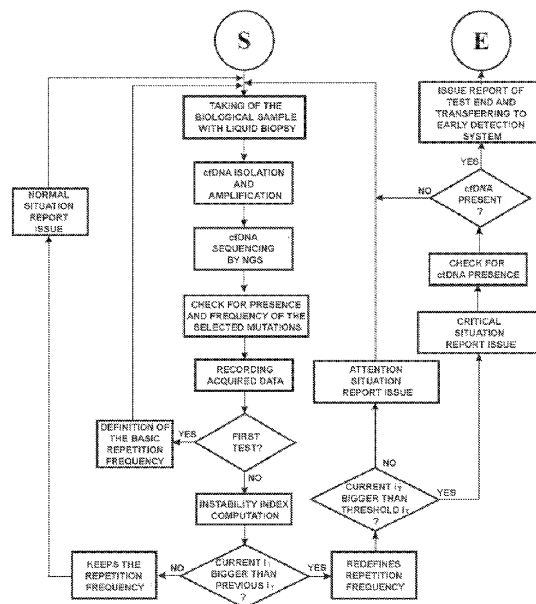
(71) Applicant: BIOSCIENCE SERVICES S.R.L. [SM/SM];
Strada Rovereta, 42, 47891 Falciano (SM).

(72) Inventor: MUCCI, Giuseppe; Strada Rovereta, 42, 47891 Falciano (SM).

(74) Agent: RUZZU, Giammario; Via Gulli, 5, 40068 San Lazzaro di Savena (IT).

(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.

(54) Title: METHOD FOR SEARCHING AND IDENTIFYING A GENETIC CONDITION PRODROMAL OF THE ONSET OF SOLID TUMORS



(57) Abstract: The method for searching and identifying a genetic condition prodromal of the onset of solid tumors in a healthy subject includes an evaluation cycle of a genetic stability or instability condition and at least one repetition cycle of said evaluation. The repetition cycles are carried out periodically on the subject, with the frequency depending on the result of the previous cycle. Each cycle includes the steps of: - taking a sample of biological material, isolating the DNA from the biological material, amplifying and sequencing the isolated DNA; - verifying the presence of mutations selected in a predetermined set of genes of the sample under consideration, said set of genes and said mutations being associated with the onset of solid tumors; - the predetermined set of genes including either a subset of the panel of genes or hotspots connected to one or more solid

(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))

tumors, or the entire panel of genes connected to solid tumors; - verifying the frequency of mutations detected for each gene and for each evaluation cycle, the mutations being selected from the aforementioned selected mutations; - recording the mutations detected for each gene or group of genes and their frequency; - defining or updating a genetic instability index of the subject, either overall (I_T) or for a single gene (I_G), for each repetition cycle, based on the frequency of mutations detected and on the basis of the increase in the frequency of mutations; - evaluating, in each repetition cycle, the subject's entry into a prodromal genetic condition upon the onset of one or more solid tumors or groups of solid tumors on the basis of a threshold value ($I_{TS,J_{GS}}$) of the genetic instability index (I_T, I_G), defined for each single gene or group of genes, being exceeded.