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Cancer Research Literatures (1)

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Abstract: Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries. This article introduces recent research reports as references in the related studies.
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Key words: cancer; life; research; literature; cell

1. Introduction

Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries. This article introduces recent research reports as references in the related studies.

The following introduces recent reports as references in the related studies.

Araujo, L. H., et al. (2015). "Impact of Pre-Analytical Variables on Cancer Targeted Gene Sequencing Efficiency." PLoS One **10**(11): e0143092.

Tumor specimens are often preserved as formalin-fixed paraffin-embedded (FFPE) tissue blocks, the most common clinical source for DNA sequencing. Herein, we evaluated the effect of pre-sequencing parameters to guide proper sample selection for targeted gene sequencing. Data from 113 FFPE lung tumor specimens were collected, and targeted gene sequencing was performed. Libraries were constructed using custom probes and were paired-end sequenced on a next generation sequencing platform. A PCR-based quality control (QC) assay was utilized to determine DNA quality, and a ratio was generated in comparison to control DNA. We observed that FFPE storage time, PCR/QC ratio, and DNA input in the library preparation were significantly correlated to most parameters of sequencing efficiency including depth of coverage, alignment rate, insert size, and read quality. A combined score using the three parameters was generated and proved highly accurate to predict sequencing metrics. We also showed wide read count variability within the genome, with worse coverage in regions of low GC content like in KRAS. Sample quality and GC content had independent effects on sequencing depth, and the worst results were observed in regions of low GC content in samples with poor quality. Our data confirm that FFPE samples are a reliable source for targeted gene sequencing in cancer, provided adequate sample quality controls are exercised. Tissue quality should be routinely assessed for pre-analytical factors, and sequencing depth may be limited in genomic regions of low GC content if suboptimal samples are utilized.

Caswell-Jin, J. L., et al. (2018). "Racial/ethnic differences in multiple-gene sequencing results for hereditary cancer risk." Genet Med **20**(2): 234-239.

Purpose: We examined racial/ethnic differences in the usage and results of germ-line multiple-gene sequencing (MGS) panels to evaluate hereditary cancer risk. MethodsWe collected genetic testing results and clinical information from 1,483 patients who underwent MGS at Stanford University between 1 January 2013 and 31 December 2015.ResultsAsians and Hispanics presented for MGS at younger ages than whites (48 and 47 vs. 55; P = 5E-16 and 5E-14). Across all panels, the rate of pathogenic variants (15%) did not differ significantly between racial groups. Rates by gene did differ: in particular, a higher percentage of whites than nonwhites carried pathogenic CHEK2 variants (3.8% vs. 1.0%; P = 0.002). The rate of a variant of uncertain significance (VUS) result was higher in nonwhites than whites (36% vs. 27%; P = 2E-4). The probability of a VUS

increased with increasing number of genes tested; this effect was more pronounced for nonwhites than for whites (1.1% absolute difference in VUS rates testing BRCA1/2 vs. 8% testing 13 genes vs. 14% testing 28 genes), worsening the disparity. ConclusionIn this diverse cohort undergoing MGS testing, pathogenic variant rates were similar between racial/ethnic groups. By contrast, VUS results were more frequent among nonwhites, with potential significance for the impact of MGS testing by race/ethnicity.

Estrada, S. S., et al. (2015). "Next-Generation Gene Sequencing: Looking Beyond Hereditary Breast and Ovarian Cancer." Oncol Nurs Forum **42**(6): 691-694.

Oncology nurses have long been aware of the significance of recognizing patients' hereditary risk of cancer. Obtaining an accurate family history is an integral part of patient assessment and has helped to guide referrals for genetic counseling and testing for hereditary breast and ovarian cancer syndrome (HBOC) and Lynch syndrome.

Huang, D., et al. (2004). "High-throughput gene sequencing assay development for hereditary nonpolyposis colon cancer." Clin Colorectal Cancer **4**(4): 275-279.

Hereditary nonpolyposis colorectal cancer (HNPCC) is the most common hereditary colon cancer syndrome and is responsible for as many as 10% of all colorectal cancers. Hereditary nonpolyposis colorectal cancer is autosomally dominant with a prevalence of 1 in 200-2000 and exhibits incomplete penetrance. Affected individuals have an approximately 70% lifetime risk of colon cancer with a mean age of onset of 44 years and an approximately 40% lifetime risk of endometrial cancer. At least 5 mismatch repair genes (MLH1, MSH2, MSH6, PMS1, PMS2) have been implicated in HNPCC; however, no predominant mutations were found in these genes. Mutation detection by direct sequencing has proven to be the most sensitive method. We have developed high-throughput full-length sequencing assays of the MLH1, MSH2, and MSH6 genes. These 3 genes account for approximately 90% of all germline mutations found in HNPCC. In our assays, 19 exons of MLH1, 16 exons of MSH2, 10 exons of MSH6, and the adjacent splice sites were amplified using polymerase chain reaction and loaded onto a capillary sequencing machine. Results were analyzed using sequence analysis software and stored in a relational database. Our assay method was validated using 15 affected patients and normal controls. It is anticipated that our high-throughput assay technique will provide accurate diagnoses for patients at risk for HNPCC and thereby facilitate early curative intervention.

Jang, J. H., et al. (2012). "Spectra of BRCA1 and BRCA2 mutations in Korean patients with breast cancer: the importance of whole-gene sequencing." J Hum Genet **57**(3): 212-215.

The frequencies and spectra of germline mutations in the BRCA1 and BRCA2 genes vary among populations. In the present study, the mutation spectra of the BRCA1/BRCA2 genes in Korean breast cancer patients were investigated using whole-gene sequencing method. A total of 134 unrelated Korean breast cancer patients who were identified as being at high risk of carrying BRCA1/BRCA2 mutations were included. PCR amplification and direct sequencing were performed covering all exons and flanking intronic sequences of the BRCA1/BRCA2 genes. A total of 26 mutations were detected in 31 of 134 patients (23.1%). The mutation detection rate in the present study is higher than those of previous studies using screening methods (2.5-11.3%) and similar to that of a recent study, which used whole-gene sequencing (21.2%). The BRCA2: c.7480C>T mutation, which has been suggested to be a founder mutation in Koreans, was detected in only one patient. Five mutations were recurrent but observed in no more than two patients. Given that the mutation detection rates using whole-gene sequencing were much higher than for screening methods and that there were no consistent observations of founder mutations, whole-gene sequencing of both BRCA1 and BRCA2 genes should be the method of choice to identify mutations in high-risk Korean patients.

Kim, H. J., et al. (2012). "Detection and comparison of peptide nucleic acid-mediated real-time polymerase chain reaction clamping and direct gene sequencing for epidermal growth factor receptor mutations in patients with non-small cell lung cancer." Lung Cancer **75**(3): 321-325.

EGFR tyrosine kinase inhibitors (EGFR-TKIs) are recommended as first-line therapy in patients with advanced, recurrent, or metastatic non-squamous non-small cell lung cancer (NSCLC) that have active EGFR mutations. The importance of rapid and sensitive methods for the detection of EGFR mutations is emphasized. The aim of this study is to examine the EGFR mutational status by both direct DNA sequencing and peptide nucleic acid (PNA)-mediated real-time PCR clamping and to evaluate the correlation between the EGFR mutational status and the clinical response to EGFR-tyrosine kinase inhibitors. Clinical specimens from 240 NSCLC patients were analyzed for EGFR mutations in exons 18, 19, 20 and 21. All clinical data and tumor specimens were obtained from 8 centers of the Korean Molecular Lung Cancer Group (KMLCG). After genomic DNA was extracted from paraffin-embedded tissue specimens, we performed

PNA-mediated real-time PCR clamping and direct DNA sequencing for the detection of EGFR mutations. Of 240 tumor samples, PNA-mediated PCR clamping was used to detect genomic alterations in 83 (34.6%) samples, including 61 identified by sequencing and 22 additional samples (10 in exon 19, 9 in exon 21, and 3 in both exons); direct DNA sequencing was used to identify a total of 63 (26.3%) mutations that contained 40 deletion mutations in exon 19 (63.5%) and 18 substitution mutations (28.6%) in exon 21. PNA-mediated PCR clamping was used to identify more mutations than clinical direct sequencing, whereas clinical outcomes were not significantly different between the groups harboring activating mutations detected by each method. These data suggest that PNA-mediated real-time PCR clamping exhibits high sensitivity and is a simple procedure relative to direct DNA sequencing that is a useful screening tool for the detection of EGFR mutations in clinical settings.

Kurian, A. W., et al. (2014). "Clinical evaluation of a multiple-gene sequencing panel for hereditary cancer risk assessment." J Clin Oncol **32**(19): 2001-2009.

PURPOSE: Multiple-gene sequencing is entering practice, but its clinical value is unknown. We evaluated the performance of a customized germline-DNA sequencing panel for cancer-risk assessment in a representative clinical sample. METHODS: Patients referred for clinical BRCA1/2 testing from 2002 to 2012 were invited to donate a research blood sample. Samples were frozen at -80 degrees C, and DNA was extracted from them after 1 to 10 years. The entire coding region, exon-intron boundaries, and all known pathogenic variants in other regions were sequenced for 42 genes that had cancer risk associations. Potentially actionable results were disclosed to participants. RESULTS: In total, 198 women participated in the study: 174 had breast cancer and 57 carried germline BRCA1/2 mutations. BRCA1/2 analysis was fully concordant with prior testing. Sixteen pathogenic variants were identified in ATM, BLM, CDH1, CDKN2A, MUTYH, MLH1, NBN, PRSS1, and SLX4 among 141 women without BRCA1/2 mutations. Fourteen participants carried 15 pathogenic variants, warranting a possible change in care; they were invited for targeted screening recommendations, enabling early detection and removal of a tubular adenoma by colonoscopy. Participants carried an average of 2.1 variants of uncertain significance among 42 genes. CONCLUSION: Among women testing negative for BRCA1/2 mutations, multiple-gene sequencing identified 16 potentially pathogenic mutations in other genes (11.4%; 95% CI, 7.0% to 17.7%), of which 15 (10.6%; 95% CI, 6.5% to 16.9%) prompted consideration of a change in care, enabling early detection of a precancerous colon polyp. Additional studies are required to quantify the penetrance of identified mutations and determine clinical utility. However, these results suggest that multiple-gene sequencing may benefit appropriately selected patients.

Kwong, A., et al. (2012). "Identification of BRCA1/2 founder mutations in Southern Chinese breast cancer patients using gene sequencing and high resolution DNA melting analysis." PLoS One **7**(9): e43994.

BACKGROUND: Ethnic variations in breast cancer epidemiology and genetics have necessitated investigation of the spectra of BRCA1 and BRCA2 mutations in different populations. Knowledge of BRCA mutations in Chinese populations is still largely unknown. We conducted a multi-center study to characterize the spectra of BRCA mutations in Chinese breast and ovarian cancer patients from Southern China. METHODOLOGY/PRINCIPAL FINDINGS: A total of 651 clinically high-risk breast and/or ovarian cancer patients were recruited from the Hong Kong Hereditary Breast Cancer Family Registry from 2007 to 2011. Comprehensive BRCA1 and BRCA2 mutation screening was performed using bi-directional sequencing of all coding exons of BRCA1 and BRCA2. Sequencing results were confirmed by in-house developed full high resolution DNA melting (HRM) analysis. Among the 451 probands analyzed, 69 (15.3%) deleterious BRCA mutations were identified, comprising 29 in BRCA1 and 40 in BRCA2. The four recurrent BRCA1 mutations (c.470_471delCT, c.3342_3345delAGAA, c.5406+1_5406+3delGTA and c.981_982delAT) accounted for 34.5% (10/29) of all BRCA1 mutations in this cohort. The four recurrent BRCA2 mutations (c.2808_2811delACAA, c.3109C>T, c.7436_7805del370 and c.9097_9098insA) accounted for 40% (16/40) of all BRCA2 mutations. Haplotype analysis was performed to confirm 1 BRCA1 and 3 BRCA2 mutations are putative founder mutations. Rapid HRM mutation screening for a panel of the founder mutations were developed and validated. CONCLUSION: In this study, our findings suggest that BRCA mutations account for a substantial proportion of hereditary breast/ovarian cancer in Southern Chinese population. Knowing the spectrum and frequency of the founder mutations in this population will assist in the development of a cost-effective rapid screening assay, which in turn facilitates genetic counseling and testing for the purpose of cancer risk assessment.

Lin, P. H., et al. (2016). "Multiple gene sequencing for risk assessment in patients with early-onset or familial breast cancer." Oncotarget **7**(7): 8310-8320.

Since BRCA mutations are only responsible for 10-20% of cases of breast cancer in patients with early-onset or a family history and since next-

generation sequencing technology allows the simultaneous sequencing of a large number of target genes, testing for multiple cancer-predisposing genes is now being considered, but its significance in clinical practice remains unclear. We then developed a sequencing panel containing 68 genes that had cancer risk association for patients with early-onset or familial breast cancer. A total of 133 patients were enrolled and 30 (22.6%) were found to carry germline deleterious mutations, 9 in BRCA1, 11 in BRCA2, 2 in RAD50, 2 in TP53 and one each in ATM, BRIP1, FANCI, MSH2, MUTYH, and RAD51C. Triple-negative breast cancer (TNBC) was associated with the highest mutation rate (45.5%, p = 0.025). Seven of the 9 BRCA1 mutations and the single FANCI mutation were in the TNBC group; 9 of the 11 BRCA2, 1 of the 2 RAD50 as well as BRIP1, MSH2, MUTYH, and RAD51C mutations were in the hormone receptor (HR)(+)Her2(-) group, and the other RAD50, ATM, and TP53 mutations were in the HR(+)Her2(+) group. Mutation carriers were considered as high-risk to develop malignancy and advised to receive cancer screening. Screening protocols of non-BRCA genes were based on their biologic functions; for example, patients carrying RAD51C mutation received a screening protocol similar to that for BRCA, since BRCA and RAD51C are both involved in homologous recombination. In conclusion, we consider that multiple gene sequencing in cancer risk assessment is clinically valuable.

Sato, K. A., et al. (2016). "Individualized Mutation Detection in Circulating Tumor DNA for Monitoring Colorectal Tumor Burden Using a Cancer-Associated Gene Sequencing Panel." PLoS One **11**(1): e0146275.

BACKGROUND: Circulating tumor DNA (ctDNA) carries information on tumor burden. However, the mutation spectrum is different among tumors. This study was designed to examine the utility of ctDNA for monitoring tumor burden based on an individual mutation profile. METHODOLOGY: DNA was extracted from a total of 176 samples, including pre- and post-operational plasma, primary tumors, and peripheral blood mononuclear cells (PBMC), from 44 individuals with colorectal tumor who underwent curative resection of colorectal tumors, as well as nine healthy individuals. Using a panel of 50 cancer-associated genes, tumor-unique mutations were identified by comparing the single nucleotide variants (SNVs) from tumors and PBMCs with an Ion PGM sequencer. A group of the tumor-unique mutations from individual tumors were designated as individual marker mutations (MMs) to trace tumor burden by ctDNA using droplet digital PCR (ddPCR). From these experiments, three major objectives were assessed: (a) Tumor-unique mutations; (b) mutation spectrum of a tumor; and (c) changes in allele frequency of the MMs in ctDNA after curative resection of the tumor. RESULTS: A total of 128 gene point mutations were identified in 27 colorectal tumors. Twenty-six genes were mutated in at least 1 sample, while 14 genes were found to be mutated in only 1 sample, respectively. An average of 2.7 genes were mutated per tumor. Subsequently, 24 MMs were selected from SNVs for tumor burden monitoring. Among the MMs found by ddPCR with > 0.1% variant allele frequency in plasma DNA, 100% (8 out of 8) exhibited a decrease in post-operation ctDNA, whereas none of the 16 MMs found by ddPCR with < 0.1% variant allele frequency in plasma DNA showed a decrease. CONCLUSIONS: This panel of 50 cancer-associated genes appeared to be sufficient to identify individual, tumor-unique, mutated ctDNA markers in cancer patients. The MMs showed the clinical utility in monitoring curatively-treated colorectal tumor burden if the allele frequency of MMs in plasma DNA is above 0.1%.

Saunders, M. E., et al. (1999). "Patterns of p53 gene mutations in head and neck cancer: full-length gene sequencing and results of primary radiotherapy." Clin Cancer Res **5**(9): 2455-2463.

p53 gene alterations are common in head and neck cancers, but their prognostic value has not been clearly established. Despite evidence in other cancers that sequencing of the entire p53 coding region provides prognostic information, full-length p53 gene sequencing has rarely been performed in head and neck cancers. In this study, p53 was assessed in a series of 42 pretreatment biopsies from patients with laryngeal carcinomas by full-length gene sequencing and by immunohistochemistry (IHC). Associations among p53 genotype, protein expression, and local recurrence were assessed in 35 irradiated patients followed for a minimum of 5 years. DNA was extracted from formalin-fixed, paraffin-embedded biopsies, and exons 2-11 of the p53 gene were individually amplified by PCR and then directly sequenced. IHC was performed to detect mutant and wild-type p53 protein using the DO7 monoclonal antibody. p21 protein expression was assessed using the EA1 monoclonal antibody. Twenty genetic alterations were observed in 42 tumors (48%). Four of these alterations (20%) occurred outside exons 5-8. There was a significant association between p53 gene and protein status (chi2 = 4.18, P = 0.04), although the correlation was weak (phi coefficient = -0.327). Although local relapse following radiation was significantly associated with nodal status, no correlations were observed between p53 status (gene or IHC) and local recurrence following radiation therapy, based on the Kaplan-Meier method. These results show that p53 mutations are common in laryngeal carcinomas and that a proportion occur outside traditionally examined regions. The lack of correlation

between p53 status and local control suggests that this marker is not as powerful as traditional prognostic factors, such as lymph node status.

Silvestri, V., et al. (2017). "Whole-exome sequencing and targeted gene sequencing provide insights into the role of PALB2 as a male breast cancer susceptibility gene." Cancer **123**(2): 210-218.

BACKGROUND: Male breast cancer (MBC) is a rare disease whose etiology appears to be largely associated with genetic factors. BRCA1 and BRCA2 mutations account for about 10% of all MBC cases. Thus, a fraction of MBC cases are expected to be due to genetic factors not yet identified. To further explain the genetic susceptibility for MBC, whole-exome sequencing (WES) and targeted gene sequencing were applied to high-risk, BRCA1/2 mutation-negative MBC cases. METHODS: Germ-line DNA of 1 male and 2 female BRCA1/2 mutation-negative breast cancer (BC) cases from a pedigree showing a first-degree family history of MBC was analyzed with WES. Targeted gene sequencing for the validation of WES results was performed for 48 high-risk, BRCA1/2 mutation-negative MBC cases from an Italian multicenter study of MBC. A case-control series of 433 BRCA1/2 mutation-negative MBC and female breast cancer (FBC) cases and 849 male and female controls was included in the study. RESULTS: WES in the family identified the partner and localizer of BRCA2 (PALB2) c.419delA truncating mutation carried by the proband, her father, and her paternal uncle (all affected with BC) and the N-acetyltransferase 1 (NAT1) c.97C>T nonsense mutation carried by the proband's maternal aunt. Targeted PALB2 sequencing detected the c.1984A>T nonsense mutation in 1 of the 48 BRCA1/2 mutation-negative MBC cases. NAT1 c.97C>T was not found in the case-control series. CONCLUSIONS: These results add strength to the evidence showing that PALB2 is involved in BC risk for both sexes and indicate that consideration should be given to clinical testing of PALB2 for BRCA1/2 mutation-negative families with multiple MBC and FBC cases. Cancer 2017;123:210-218. (c) 2016 American Cancer Society.

Takahashi, M., et al. (2017). "OLA1 gene sequencing in patients with BRCA1/2 mutation-negative suspected hereditary breast and ovarian cancer." Breast Cancer **24**(2): 336-340.

BACKGROUND: Of individuals with suspected hereditary breast and ovarian cancer (HBOC), approximately 30-70 % do not harbor mutations in either BRCA1 or BRCA2 gene, which suggests that these individuals have other genetic or epigenetic alterations that could lead to the onset of this hereditary disease. We have recently identified OLA1 as a novel BRCA1/BARD1-interacting protein. In the present study, we aimed to elucidate whether any genetic mutations in OLA1 are detected among patients with suspected HBOC without BRCA1 or BRCA2 mutations. METHODS: Among 53 patients with suspected HBOC enrolled at Hoshi General Hospital, 23 patients without any BRCA1 or BRCA2 mutations were analyzed for OLA1 mutations. Genomic DNA was extracted from the peripheral blood samples. PCR and Sanger sequencing were performed to elucidate whether there were any mutations in any of the ten exons and flanking introns of the OLA1 gene. RESULTS: No germline sequence variation was detected in the OLA1 gene among the 23 patients enrolled in this study. CONCLUSIONS: No germline mutations were found in the OLA1 gene among the cohort of patients with suspected HBOC without BRCA1 or BRCA2 mutations. Further studies are needed to clarify whether other mutations/epigenetic alterations are involved in the pathogenesis of BRCA1 or BRCA2 mutation-negative inherited disease with breast or ovarian cancer.

Takahashi, Y., et al. (2003). "Clinical application of oligonucleotide probe array for full-length gene sequencing of TP53 in colon cancer." Oncology **64**(1): 54-60.

OBJECTIVE: TP53 mutations are the most frequent genetic alterations in colon cancer. We studied whether the recently developed oligonucleotide microarray technique, GeneChip p53 assay, can be applied to sensitive detection of TP53 gene mutations in surgical specimens from colon cancer patients. METHODS: TP53 gene mutations in exons 2-11 in 20 colon cancers and the corresponding histopathologically normal mucosa at the surgical margins were assessed by GeneChip p53 assay, and the results were further evaluated by direct sequencing of the involved exon or by mutant-allele-specific amplification (MASA). The expression of TP53 protein was also evaluated immunohistochemically and the result was compared with the gene alteration. RESULTS: The GeneChip p53 assay detected TP53 mutations in 65% of primary cancers; 61% of the mutations were within the evolutionarily conserved regions, and 46% of the mutations were within the zinc-binding domains (regions of loop 2 and loop 3). Direct sequencing confirmed these mutations. Immunohistochemical examination detected TP53 protein overexpression in 47% of primary cancers, but this protein did not accumulate with all types of TP53 mutations. In addition, the GeneChip assay detected a mutation identical to that in the primary tumor in 2 samples from the surgical margins, and MASA confirmed both mutations, implying the presence of occult cancer cells. CONCLUSION: The GeneChip p53 assay is sufficiently sensitive to detect TP53

mutations in surgical specimens from colon cancers and may be applicable to screening examination in clinical laboratories as a routine procedure.

Vysotskaia, V. S., et al. (2017). "Development and validation of a 36-gene sequencing assay for hereditary cancer risk assessment." PeerJ **5**: e3046.

The past two decades have brought many important advances in our understanding of the hereditary susceptibility to cancer. Numerous studies have provided convincing evidence that identification of germline mutations associated with hereditary cancer syndromes can lead to reductions in morbidity and mortality through targeted risk management options. Additionally, advances in gene sequencing technology now permit the development of multigene hereditary cancer testing panels. Here, we describe the 2016 revision of the Counsyl Inherited Cancer Screen for detecting single-nucleotide variants (SNVs), short insertions and deletions (indels), and copy number variants (CNVs) in 36 genes associated with an elevated risk for breast, ovarian, colorectal, gastric, endometrial, pancreatic, thyroid, prostate, melanoma, and neuroendocrine cancers. To determine test accuracy and reproducibility, we performed a rigorous analytical validation across 341 samples, including 118 cell lines and 223 patient samples. The screen achieved 100% test sensitivity across different mutation types, with high specificity and 100% concordance with conventional Sanger sequencing and multiplex ligation-dependent probe amplification (MLPA). We also demonstrated the screen's high intra-run and inter-run reproducibility and robust performance on blood and saliva specimens. Furthermore, we showed that pathogenic Alu element insertions can be accurately detected by our test. Overall, the validation in our clinical laboratory demonstrated the analytical performance required for collecting and reporting genetic information related to risk of developing hereditary cancers.

The above contents are the collected information from Internet and public resources to offer to the people for the convenient reading and information disseminating and sharing.

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